

AEROSPACE MEDICINE AND BIOLOGY

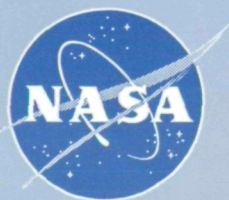
A CONTINUING BIBLIOGRAPHY WITH INDEXES

(NASA-SP-7011(403)) AEROSPACE
MEDICINE AND BIOLOGY: A CONTINUING
BIBLIOGRAPHY WITH INDEXES
(SUPPLEMENT 403) (NASA) 101 p

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NASA SP-7011 (403)

July 1995

AEROSPACE MEDICINE AND BIOLOGY

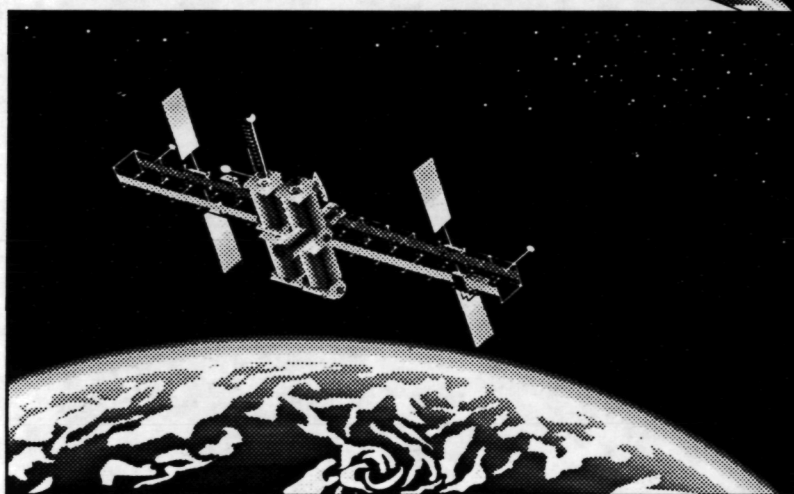
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INTRODUCTION

This issue of *Aerospace Medicine and Biology* (NASA SP-7011) lists 217 reports, articles, and other documents recently announced in the NASA STI Database. The first issue of *Aerospace Medicine and Biology* was published in July 1964.

Accession numbers cited in this issue include:

Scientific and Technical Aerospace Reports (STAR) (N-10000 Series)

Open Literature (A-60000 Series)

N95-22478 — N95-24194

A95-73327 — A95-77372

In its subject coverage, *Aerospace Medicine and Biology* concentrates on the biological, physiological, psychological, and environmental effects to which humans are subjected during and following simulated or actual flight in the Earth's atmosphere or in interplanetary space. References describing similar effects on biological organisms of lower order are also included. Such related topics as sanitary problems, pharmacology, toxicology, safety and survival, life support systems, exobiology, and personnel factors receive appropriate attention. Applied research receives the most emphasis, but references to fundamental studies and theoretical principles related to experimental development also qualify for inclusion.

Each entry in the publication consists of a standard bibliographic citation accompanied, in most cases, by an abstract. The listing of the entries is arranged by *STAR* categories 51 through 55, the Life Sciences division. The citations include the original accession numbers from the NASA STI Database.

Seven indexes—subject, personal author, corporate source, foreign technology, contract number, report number, and accession number—are included.

A cumulative index for 1995 will be published in early 1996.

The NASA CASI price code table, addresses of organizations, and document availability information are located at the back of this issue.



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TYPICAL REPORT CITATION AND ABSTRACT

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ACCESSION NUMBER → N95-10863*# National Aeronautics and Space Administration. ← **CORPORATE SOURCE**
Ames Research Center, Moffett Field, CA.

TITLE → **BIOTELEMETRY IMPLANT VOLUME AND WEIGHT IN RATS:
A PILOT STUDY REPORT**

AUTHOR → CHRIS J. SOMPS May 1994 19 p ← **PUBLICATION DATE**

CONTRACT NUMBER → (Contract RTOP 545-20-01)

REPORT NUMBERS → (NASA-TM-108812; A-94059; NAS 1.15:108812) Avail: CASI HC ← **AVAILABILITY AND PRICE CODE**
A03/MF A01

This paper reports the results of a pilot study in which a 240-gram rat was implanted for 41 days with biotelemetry devices weighing a total of 36 gm (18 cc). The implanted animal showed no differences in weight gain, food and water consumption, and postnecropsy organ weights when compared to both an unoperated control animal and an animal that underwent surgery but did not receive an implant. The implanted animal also had temperature and activity rhythms similar to those reported using much smaller implants. Thus, this pilot study showed that a 240-gm rat could be implanted with biotelemetry devices weighing nearly 15 percent of body weight without significant changes in health or behavior. A larger study involving more animals and similar implant sizes is recommended.

Author

TYPICAL JOURNAL ARTICLE CITATION AND ABSTRACT

NASA SPONSORED

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ACCESSION NUMBER → A95-63745* National Aeronautics and Space Administration. John F. ← **CORPORATE SOURCE**
Kennedy Space Center, Cocoa Beach, FL.

TITLE → **THE ORIGIN AND EARLY EVOLUTION OF ISSOL**

AUTHOR → RICHARD S. YOUNG NASA, Kennedy Space Center, Cocoa Beach, ← **AUTHORS' AFFILIATION**
FL, US ISSOL Meeting, 7th, Barcelona, Spain, July 4-9, 1993.

PRIMARY DOCUMENT → A95-63744 Origins of Life and Evolution of the Biosphere (ISSN 0169- ← **JOURNAL TITLE**
6149) vol. 24, no. 2-4. June 1994 p. 83 ← **PUBLICATION DATE**
Copyright

This is a discussion of the beginnings of the International Society for the Study of the Origin of Life (ISSOL)—how it came to be and the people responsible for it. It will include the early meetings on the subject of the Origin of Life which led to the formation of the Society. It will discuss the genesis of the interest of NASA in such a program and how the Exobiology Program got started, leading up to the Viking Program and the early exploration of Mars. Photographs of early meetings and the scientists involved will be included.

Author (Herner)

AEROSPACE MEDICINE AND BIOLOGY

A Continuing Bibliography (Suppl. 403)

July 1995

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LIFE SCIENCES (GENERAL)

A95-73341

ELECTRICAL MODEL FOR ION CHANNELS IN EXCITABLE MEMBRANES

K. H. NORIAN Lehigh Univ, Bethlehem, PA, United States *Journal of Materials Science Letters* (ISSN 0261-8028) vol. 13, no. 8 April 15, 1994 p. 569-572 refs (BTN-94-EIX94371346929) Copyright

The changes in permeability, to intracellular or extracellular ions, of the electrically excitable membrane that envelope nerve cells allow the propagation of electrical impulses along nerves. Permeability depends upon voltage-activated channels, which open and close (switch) to control the flow of either Na⁺ or K⁺ ions across the membrane. For those interested in describing the electrical properties of biological membranes, no model exists to account for the mechanism that triggers channel switching. An electrical model is presented here for the switching of the channels that control the flow of Na⁺ and K⁺ ions across the membrane. EI

A95-74286

SIMULTANEOUS IN VIVO MEASUREMENTS OF HbO₂ SATURATION AND PCR KINETICS AFTER EXERCISE IN NORMAL HUMANS

KEVIN K. MCCULLY, STEFANO IOTTI, KEITH KENDRICK, ZHIYUE WANG, JOEL D. POSNER, JACK LEIGH, JR., and BRITTON CHANCE *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 5-10 (HTN-95-A0585) Copyright

Simultaneous measurements of phosphocreatine (PCr) and oxyhemoglobin (HbO₂) saturation were made during recovery from exercise in calf muscles of five male subjects. PCr was measured using magnetic resonance spectroscopy in a 2.0-T 78-cm-bore magnet with a 9-cm-diam surface coil. Relative HbO₂ saturation was measured as the difference in absorption of 750- and 850-nm light with use of near-infrared spectroscopy. The light source and detectors were 3 cm apart. Exercise consisted of isokinetic plantar flexion in a supine position. Two 5-min submaximal protocols were performed with PCr depletion to 60% of resting values and with pH values of greater than 7.0. Then two 1-min protocols of rapid plantar flexion were performed to deplete PCr values to 5 - 20% of resting values with pH values of less than 6.8. Areas of PCr peaks (every 8 s) and HbO₂ saturation (every 1 s) were fit to a monoexponential function, and a time constant was calculated. The PCr time constant was larger after maximal exercise than after submaximal exercise, which is consistent with the effects of low pH on PCr recovery. HbO₂ resaturation approximated submaximal PCr recovery and was not different between maximal and submaximal exercise. We conclude that magnetic resonance spectroscopy measurements of PCr recovery and near-infrared spectroscopy measurements of recovery of HbO₂ saturation provide similar information as long as muscle pH remains near 7.0. Author (Herner)

A95-74287

MAXIMAL SKIN BLOOD FLOW IS DECREASED IN ELDERLY MEN

G. ALEC ROOKE, MARGARET V. SAVAGE, and GEORGE L. BRENGELMANN *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 11-14 Research sponsored by American Federation for Aging Research and John A. Hartford Foundation (Contract(s)/Grant(s): NIH-HL-16910) (HTN-95-A0586) Copyright

When subjected to total body heating and exercise, skin blood flow does not increase as much in elderly as in young subjects. It is not known whether this age-related decline is due to the autonomic dysfunction that develops in the elderly or to changes at the level of the blood vessels of the skin. We used local heating of the forearm to quantify the intrinsic ability of the cutaneous vasculature to dilate in seven young men (avg age 31 yr) and seven elderly men (avg age 71 yr). A water spray was used to maintain a neutral skin temperature of 32 - 35 C for greater than 10 min, followed by 60 min of a 42 C skin temperature to induce maximal skin blood flow. Forearm blood flow was measured by venous occlusion plethysmography with a mercury-in-Silastic circumference gauge. At the neutral skin temperature, forearm blood flows in the elderly subjects were comparable to those in the young subjects: 3.0 +/- 0.5 vs. 2.8 +/- 1.0 ml/min/100 ml. During the last 10 min of heating, however, blood flows were much lower in the elderly than in the young subjects: 11.1 +/- 2.7 vs. 19.9 +/- 5.2 ml/min/100 ml. We conclude that aging results in a reduction of the maximal conductance of the cutaneous vasculature. Author (Herner)

A95-74288

EFFECT OF GROWTH HORMONE ADMINISTRATION AND TREADMILL EXERCISE ON THE BODY COMPOSITION OF RATS

JAMES K. YEH, JOHN F. ALOIA, MENG MENG CHEN, and SHARON SPRINTZ *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 23-29 (HTN-95-A0587) Copyright

The aim of this study was to compare the effects of growth hormone administration and treadmill exercise on bone mass, body fat mass, and fat-free mass. Forty female rats aged 14 mo were divided into control, ovine growth hormone (GH) administration, treadmill exercise (EX), and EX + GH groups. Noninvasive total body electrical conductivity and dual X-ray absorptiometry techniques were used to assess the body fat content, fat-free mass, and tibial and L(sub 4) vertebral bone mineral content of each experimental animal at weeks 0, 9, and 16. The age-related increase in body fat mass was suppressed in the GH group, and the fat-free mass and L(sub 4) bone mass were higher in the GH group than in the control group. Conversely, in the EX group there was no gain in body fat mass and no significant change in fat-free mass or vertebral bone mass. The tibial bone mass increased in both the GH and EX groups; however, the time response to the two interventions appeared to differ. In the EX + GH group there was no further enhancement of the anabolic effect on the tibial bone mass. The effect of growth hormone administration on body fat content and bone mass is distinct from that of treadmill exercise. Author (Herner)

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A95-74289

SITES OF VASODILATION BY INHALED NITRIC OXIDE VS. SODIUM NITROPRUSSIDE IN ENDOTHELIN-CONSTRICTED ISOLATED RAT LUNGS

C. M. ROOS Virginia Univ., Charlottesville, VA, US, G. F. RICH Virginia Univ., Charlottesville, VA, US, D. R. UNCLES Virginia Univ., Charlottesville, VA, US, M. O. DAUGHERTY Virginia Univ., Charlottesville, VA, US, and D. U. FRANK Virginia Univ., Charlottesville, VA, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 51-57 Research sponsored by Virginia Heart Association (HTN-95-A0588) Copyright

We localized the sites of vasodilation of inhaled nitric oxide (NO), a selective pulmonary vasodilator, and sodium nitroprusside (SNP) in isolated rat lungs. The sites were determined by analyzing the arterial, venous, and double-occlusion data with a two-resistor (small arteries and veins) three-capacitor (large arteries, large veins, and capillaries) model of the pulmonary vascular bed. Inhaled NO (170 and 670 ppm) and SNP decreased the small-artery resistance by 7.4 ± 1.6 , 17.2 ± 2.2 , 14.2 ± 2.8 , and $21.4 \pm 3.4\%$ and the small-vein resistance by 13.5 ± 3.2 , 20.3 ± 3.4 , and $9.3 \pm 3.3\%$, respectively, in blood-perfused lungs. Similar results were observed in Krebs-perfused lungs. Capillary compliance was unaffected by inhaled NO and SNP. SNP increased the large-artery capacitance by 40.0 ± 8.6 and $69.3 \pm 9.7\%$, whereas inhaled NO had no effect. SNP increases the large-vein capacitance by 31.0 ± 8.7 and $48.0 \pm 10.7\%$, whereas inhaled NO had no effect in blood-perfused lungs. However, in Krebs-perfused lungs inhaled NO and SNP increased the large-vein capacitance by 43.3 ± 11.9 , 41.4 ± 14.2 , and $44.2 \pm 11.0\%$. In conclusion, in blood-perfused isolated rat lungs inhaled NO and SNP dilate small-resistance arteries and veins, whereas SNP but not inhaled NO dilates larger capacitance arteries and veins. Furthermore, blood appears to prevent the downstream vasodilation by inhaled NO on larger capacitance pulmonary veins. Author (Hemer)

A95-74290* National Aeronautics and Space Administration. Ames Research Center, Moffett Field, CA.

ADAPTATION OF RAT SOLEUS MUSCLES TO 4 WK OF INTERMITTENT STRAIN

W. T. STAUBER West Virginia Univ. Health Sciences Center, Morgantown, WV, US, G. R. MILLER West Virginia Univ. Health Sciences Center, Morgantown, WV, US, J. G. GRIMMETT West Virginia Univ. Health Sciences Center, Morgantown, WV, US, and K. K. KNACK West Virginia Univ. Health Sciences Center, Morgantown, WV, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 58-62

(Contract(s)/Grant(s): NAG2-590; NIH-R01-OHAR-02918) (HTN-95-A0589) Copyright

The effect of repeated strains on rat soleus muscles was investigated by stretching active muscles 3 times/wk for 4 wk with two different methods of stretching. The adaptation of myofibers and noncontractile tissue was followed by histochemical techniques and computer-assisted image analysis. Muscle hypertrophy was seen in the slow-stretched muscles, which increased in mass by 13% and increased in myofiber cross-sectional area by 30%. In the fast-stretched muscle, mass increased by 10% but myofiber cross-sectional area actually decreased. This decrease in mean fiber area was the result of a population of very small fibers (population A) that coexisted with slightly smaller normal-sized fibers (population B). Fibers in population A did not have the distribution expected from atrophy compared with atrophic fibers from unloaded muscles; they were much smaller. In addition, there was a 44% increase in noncontractile tissue in the fast-stretched muscles. Thus, soleus muscles subjected to repeated strains respond differently to slow and fast stretching. Slow stretching results in typical muscle hypertrophy, whereas fast stretching produces somewhat larger muscles but with a mixture of small and normal-sized myofibers accompanied by a marked proliferation of noncontractile tissue. Author (Hemer)

A95-74291

EFFECTS OF HYPEROXIA ON RAT DIAPHRAGM FUNCTION

ANTONIO ANZUETO, JAMES M. BRASSARD, FRANCISCO H. ANDRADE, RICHARD A. LAWRENCE, LEO C. MAXWELL, STEPHANIE M. LEVINE, and STEPHEN G. JENKINSON Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 63-68 Research sponsored by Veterans Affairs (Contract(s)/Grant(s): NIH-HL-32824) (HTN-95-A0590) Copyright

The association of oxygen radical generation with impaired diaphragm performance has previously been reported after inspiratory resistive loading (IRL). We hypothesized that exposure of rats to normobaric hyperoxia (O₂) could produce impaired diaphragm function because of free radical production. Sprague-Dawley rats were divided into four groups. Each group was studied at rest after the O₂ exposure and then after IRL. During IRL, the animals breathed through an inspiratory resistor until they were unable to sustain greater than 70% of the maximum airway pressure. Diaphragm samples were obtained for analysis of glutathione (GSH) and glutathione disulfide (GSSG) concentrations. In vitro isometric contractile properties were also determined, including maximal tetanic tension ($P_{\text{sub o}}$) and maximal twitch tension ($P_{\text{sub t}}$), in GSSG content and in GSSG-to-GSH ratios. Hyperoxia for greater than 48 h resulted in significant decreases in $P_{\text{sub o}}$ and $P_{\text{sub t}}$ and an increase in GSSG content and in GSSG-to-GSH ratios compared with other groups. Those same animals subjected to IRL showed a further decrease in $P_{\text{sub o}}$ and $P_{\text{sub t}}$. These data suggest that free radical generation may occur in the diaphragm during a hyperoxia exposure associated with activation of the GSH redox cycle and impairment of diaphragm function.

Author (Hemer)

A95-74292

REDUCED SPONTANEOUS BAROREFLEX RESPONSE SLOPE DURING LOWER BODY NEGATIVE PRESSURE AFTER 28 DAYS OF HEAD-DOWN BED REST

R. L. HUGHSON, A. MAILLET, C. GHARIB, J. O. FORTRAT, Y. YAMAMOTO, A. PAVY-LETRAON, D. RIVIERE, and A. GUELL Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 69-77 Research sponsored by CNES, Heart and Stroke Foundation of Ontario, NSERC, and Medical Research Council of Canada

(Contract(s)/Grant(s): DRET-89-237)

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Effects of 28 days of continuous 6 deg head-down tilt bed rest on spontaneous vagally mediated baroreflex response slope were evaluated from beat-by-beat relationships between R-R interval and systolic arterial blood pressure. Twelve healthy men (age 27 - 42 yr) were assigned to either countermeasure (CM) or no-countermeasure (no-CM) groups. CM consisted of strenuous short-term exercise once per day 6 days/wk from days 7 to 28 and lower body negative pressure (LBNP) for 15 min on days 16, 18, 20, and 22-28. Spontaneous baroreflex slope was evaluated by application of linear regression to sequences of at least three beats in which systolic blood pressure and R-R interval changed in the same direction. Measurements were made pre-, mid- (day 15), and post-bed rest at rest and during progressive LBNP tests. R-R interval decreased progressively and significantly over duration of bed rest. Spontaneous baroreflex slope at rest in pre-bed rest was 18.5 ± 2.1 ms/mmHg for CM and 14.9 ± 1.6 ms/mmHg for no-CM. There was a significant reduction in baroreflex slope as a function of bed rest, and it was further reduced during LBNP. Between CM and no-CM groups differences existed, but these were present pre-bed rest and appeared unaffected by countermeasures. A linear relationship existed between baroreflex slope and R-R interval such that at -50 mmHg of LBNP in post-bed-rest tests baroreflex slopes were 5.4 ± 0.8 and 5.2 ± 1.0 ms/mmHg for CM and no-CM, respectively. Because we saw a linear reduction in spontaneous baroreflex slope as a function of the reduction in R-R interval, we hypothesize that spontaneous baroreflex slope was in part a function of background vagal activity to the heart. Author (Hemer)

A95-74293

SENSITIVITY OF MUSCLE PROTON SPIN-SPIN RELAXATION TIME AS AN INDEX OF MUSCLE ACTIVATION

GUANG YUE Arizona Univ., Tucson, AZ, US, ANDREW L. ALEXANDER Arizona Univ., Tucson, AZ, US, DOUGLASS H. LAIDLAW Arizona Univ., Tucson, AZ, US, ARTHUR F. GMITRO Arizona Univ., Tucson, AZ, US, EVAN C. UNGER Arizona Univ., Tucson, AZ, US, and ROGER M. ENOKA Arizona Univ., Tucson, AZ, US *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 84-92

(Contract(s)/Grant(s): NIH-AG-0900; NIH-NS-20544)

(HTN-95-A0592) Copyright

The purpose of this study was to determine the minimum number of contractions that are needed to detect an increase in the muscle proton spin-spin relaxation time ($T_{\text{sub } 2}$) at a given exercise intensity. Five healthy human subjects performed five sets of an exercise that included concentric and eccentric contractions of the elbow-flexor muscles with loads that were 25 or 80% of maximum. The upper arm of each subject was imaged before and immediately after each set of the exercise. Spin-echo images were collected using an extremity coil, and $T_{\text{sub } 2}$ values were calculated. The signal intensity was measured from the elbow-flexor and -extensor muscles and from the bone marrow of the humerus. With the 80% load, $T_{\text{sub } 2}$ increased in the short head of the biceps brachii after two repetitions of the elbow exercise and after five repetitions in the brachialis and the long head of the biceps brachii. With the 25% load, $T_{\text{sub } 2}$ became longer after five repetitions of the exercise for the short head of the biceps brachii and after 10 repetitions for the brachialis and the long head of the biceps brachii. $T_{\text{sub } 2}$ varied linearly with the number of contraction repetitions for each of the elbow-flexor muscles at either load. The resting $T_{\text{sub } 2}$ value was not uniformly distributed among the elbow-flexor and -extensor muscles, and the $T_{\text{sub } 2}$ after a given set of the exercise was different among the three heads of the triceps brachii. These findings suggest that (1) the sensitivity of $T_{\text{sub } 2}$ for detecting muscle activity depends on the contraction intensity, (2) within a specified range ($T_{\text{sub } 2}$) varies linearly with work performed by the muscle, and (3) recruitment of the muscle fibers is different for a given task among the compartments within the flexor or extensor muscles of the elbow joint.

Author (Hemer)

A95-74294

BICYCLE EXERCISE ENHANCES PLASMA IL-6 BUT DOES NOT CHANGE IL-1 ALPHA, IL-1 BETA, IL-6, OR TNF-ALPHA PRE-MRNA IN BMNC

HENRIK ULLUM, POUL MARTIN HAAHR, MARCUS DIAMANT, JAN PALMO, JENS HALKJAER-KRISTENSEN, and BENTE KLARLUND PEDERSEN *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 93-97 Research sponsored by Danish National Research Foundation and Danish Research Council

(HTN-95-A0593) Copyright

The present study investigated the effect of concentric exercise on cytokine plasma levels and cytokine pre-mRNA in blood mononuclear cells (BMNCs). Healthy young moderately trained men performed ergometer bicycle exercise for 1 h at 75% of maximal oxygen uptake. The levels of plasma interleukin (IL)-6 increased significantly during exercise, but plasma levels of IL-1 alpha, IL-1 beta, and tumor necrosis factor-alpha (TNF-alpha) were below the detection limit in most subjects. Pre-mRNA for IL-1 alpha, IL-1 beta, IL-6, and TNF-alpha could be detected in BMNCs, but the amounts did not change in relation to exercise. These results indicate that, although the absolute number of monocytes increases during exercise and the percentage of CD14(+)/HLA-DR(+) and CD14(+)/HLA-DR(-) monocytes increases after exercise, the increased plasma levels of IL-6 during exercise is not likely to be a result of activated monocytes in peripheral blood.

Author (Hemer)

A95-74295

SEGMENTAL BIOELECTRICAL IMPEDANCE ANALYSIS: THEORY AND APPLICATION OF A NEW TECHNIQUE

LESLIE W. ORGAN Medical Univ. of South Carolina, Charleston, SC, US, GILBERT B. BRADHAM Medical Univ. of South Carolina, Charleston, SC, US, DWIGHT T. GORE Medical Univ. of South Carolina, Charleston, SC, US, and SUSAN L. LOZIER Medical Univ. of South Carolina, Charleston, SC, US *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 98-112 (HTN-95-A0594) Copyright

Bioelectrical impedance analysis (BIA) for body composition has been based on the volume conductor model that results in the mathematical relationship $Ht(\exp 2)/R$ approx. FFM, where Ht is body height, R is whole body resistance or impedance, and FFM is fat-free mass. Although this relationship exists in the human subject, its strength and usefulness have been subject to conflicting reports. This study reassessed the theory and methodology of BIA and describes a new technique for measuring segmental impedance that may resolve some major limitations associated with the current whole body impedance methodology. By use of data from 200 adult subjects, a new theory and methodology for BIA were developed in four steps: (1) a rationale was presented for replacing the $Ht(\exp 2)/R$ model by one based on electrical resistivity, (2) a practical six-electrode technique for segmental BIA that uses only peripheral electrode sites was described, (3) prediction equations for fat weight based on the new segmental BIA technique were developed, and (4) prediction equations for fat distributions, a potential new use of impedance methodology, were developed using a new measure of fat distribution, the impedance index.

Author (Hemer)

A95-74296

AN ATP-SENSITIVE POTASSIUM CHANNEL BLOCKER DECREASES DIAPHRAGMATIC CIRCULATION IN ANESTHETIZED DOGS

A. COMTOIS, C. SINDERBY, N. COMTOIS, A. GRASSINO, and J. M. RENAUD *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 127-134 Research sponsored by Medical Research Council of Canada (HTN-95-A0595) Copyright

The goal of this study was to determine whether in the dog ATP-sensitive $K(+)$ channels blocked with glibenclamide affect diaphragmatic blood flow (phrenic arterial blood flow (dot-Qpa)) during both spontaneous breathing at rest and increased diaphragmatic activity. A control group and an experimental group were studied. During spontaneous breathing at rest, dot-Qpa was 15.0 ml/min/100 g and decreased by 5% in the presence of glibenclamide. Diaphragmatic pacing generated by phrenic nerve pacing produced an initial diaphragmatic tension-time index of 0.25 in both groups. A 50% decay in transdiaphragmatic pressure was reached at 165 s in the experimental group compared with 421 s in the control group. Diaphragmatic pacing increased dot-Qpa by 46% in the experimental group and 65% in the control group, yielding a 63% greater vascular resistance in the experimental group. Phrenic vein $K(+)$ content at rest was unchanged by the presence of glibenclamide, being 3.6 ± 0.16 mmol/l compared with 3.5 ± 0.16 mmol/l in the control group. Phrenic nerve pacing in the control group produced a 13% increase in phrenic vein $K(+)$ content, whereas in the experimental group a 16% decrease was observed. We suggest that ATP-sensitive $K(+)$ channels play an important role in the modulation of dot-Qpa.

Author (Hemer)

A95-74297

FORCE AND CONTRACTILE CHARACTERISTICS AFTER STRETCH OVERLOAD IN QUAIL ANTERIOR LATISSIMUS DORSI MUSCLE

STEPHEN E. ALWAY Ohio State Univ., Columbus, OH, US *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 135-141 Research sponsored by American Federation for Aging Research

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Stretch overload has been shown to increase muscle mass by increasing fiber size and fiber number in the anterior latissimus dorsi (ALD) of adult Japanese quail. However, the functional significance

of these changes is not known. The purpose of this study was to determine if stretch-induced hypertrophy alters function of the ALD. A tube weight corresponding to 12% of the bird's body mass was added to one wing of 12 Japanese quail for 30 days. This increased muscle mass corrected for the increase in nonmuscle tissue by 121 \pm 3%. In vitro contractile measures were made at 25 C by direct stimulation of the ALD. Fiber hypertrophy accounted for only 60% of the 95% increase in maximal force in stretched muscles. Specific tension was similar in control and experimental muscles. Stretch-enlarged muscles had significantly greater twitch half-relaxation time relative to control muscles. The maximal velocity of loaded shortening decreased from 2.6 \pm 0.4 muscle lengths/s in control muscles to 1.1 \pm 0.1 muscle lengths/s in stretched muscles. The maximal velocity of unloaded shortening decreased from 4.2 \pm 0.6 to 2.6 muscle lengths/s in stretched muscles. These data indicate that (1) twitch duration and shortening velocity are slowed in stretch hypertrophied muscle and (2) new fibers contribute to force production after 30 days of stretch overload. Author (Hemer)

A95-74298

CALCITONIN GENE-RELATED PEPTIDE MODULATES PULMONARY VASCULAR REACTIVITY IN ISOLATED RAT LUNGS

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The role of calcitonin gene-related peptide (CGRP) in modulating hypoxic pulmonary vasoconstriction was assessed. The effects of CGRP and its antagonist (CGRP-(8 - 37) on responses to acute hypoxia and angiotensin II were studied in isolated lungs of male Sprague-Dawley rats perfused with a salt solution. Rats with pulmonary hypertension, induced by simulated altitude exposure, were also used to determine the actions of CGRP in a remodeled pulmonary vascular bed. In normotensive (NT) and altitude-exposed (AE) lungs, CGRP injections (10 nM), given after stable pressor responses were attained, attenuated subsequent hypoxic pressor responses. Pretreatment with CGRP-(8 - 37) (10 nM) enhanced initial ANG II-induced pressor responses in both AE and NT lungs. CGRP-(8 - 37) pretreatment (10 nM) had little influence on the hypoxic pressor responses in either NT or AE lungs. Results indicate that CGRP modulates hypoxic pulmonary vasoconstriction and that CGRP-(8 - 37) enhances pressor responses to ANG II in NT and AE rat lungs. Author (Hemer)

A95-74299

DYNAMIC PROPERTIES OF BODY PLETHYSMOGRAPHS AND EFFECTS ON PHYSIOLOGICAL PARAMETERS

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A model incorporating compliance, resistance, inertia, and the thermal time constant of plethysmographs is used to describe the effect of its dynamic properties on measured respiratory parameters. Using numerical simulation we studied the effect of distortion of flow signals from 13 infants in whom flow and esophageal pressure had been recorded. The distortion in amplitude, shape, and timing of the recorded flow patterns was dependent on the dynamic properties of the plethysmograph. For constant-volume 'pressure' plethysmographs, errors of derived parameters such as compliance and resistance are very important if the thermal time constant is short. These errors are not corrected by calibrating the plethysmograph at the breathing frequency. Time correction of the flow signals

in volume-displacement plethysmographs gives accurate results when the plethysmograph resistance and compliance are low. Overall, a volume-displacement plethysmograph with moderately high resistance of the flowmeter, corrected for internal pressure and inertia, gives the best possible results. Author (Hemer)

A95-74300

ROLE OF EDRF IN THE REGULATION OF REGIONAL BLOOD FLOW AND VASCULAR RESISTANCE AT REST AND DURING EXERCISE IN CONSCIOUS DOGS

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The contribution of endothelium-derived relaxing factor (EDRF) to the regulation of regional vascular resistance and tissue blood flow at rest and during acute moderate exercise was studied in chronically instrumented conscious dogs. Radioactive microspheres were injected before and during exercise to measure regional blood flow. An infusion of nitro-L-arginine (L-NA), an analogue of L-arginine, was used to inhibit the synthesis of EDRF and resulted in a significant increase in mean arterial pressure, associated with significantly elevated vascular resistance in heart, skeletal muscle, renal and splanchnic circulations and with decreases in tissue blood flow in those regions at rest. Acute exercise caused a typical redistribution of blood flow, in which there was vasodilation in heart and working skeletal muscles, accompanied by vasoconstriction in kidney and splanchnic circulations. L-NA resulted in significantly elevated vascular resistance during vasodilation in heart and working skeletal muscles and also significantly increased vasoconstriction in renal cortex, stomach, pancreas, liver, and colon during exercise. Blood flows during exercise were largely unaffected by L-NA treatment. Our results suggest that whereas EDRF functions to regulate basal vascular tone and vascular resistance during exercise, EDRF has a minor role in determining the pattern of the redistribution of tissue blood flow during exercise. Author (Hemer)

A95-74301

DIFFERENT EFFECTS OF RESPIRATORY AND METABOLIC ACIDOSIS ON PREGANGLIONIC SYMPATHETIC NERVE ACTIVITY

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We studied sympathetic nerve activity (SNA) responses, recorded in multifiber preparations of left third thoracic white ramus, to respiratory or isocapnic metabolic acidosis or to CO₂ enhancement at constant pH in chloralose-anesthetized paralyzed artificially ventilated cats. Cardiopulmonary, baro-, and peripheral chemoreceptors were denervated by bilaterally cutting vagus and carotid sinus nerves. Acidosis was induced by either decreasing artificial ventilation or infusing HCl (0.5 M iv). Both respiratory and isocapnic metabolic acidosis induced a decrease in local extracellular pH, measured directly with pH-sensitive microelectrodes within medulla region containing sympathoexcitatory bulbospinal neurons. The magnitude of changes in medullary pH was independent of the way systemic acidosis was generated. Despite uniformity of changes in local medullary extracellular pH due to systemic respiratory or isocapnic metabolic acidosis, different responses were observed in preganglionic SNA. Isocapnic metabolic acidosis resulted in a slight

increase in SNA, averaging 6.4% per 0.05 systemic pH unit decrease. In contrast, respiratory acidosis induced by decreasing artificial ventilation produced a more pronounced increase of SNA, reaching peak changes of approximately 70% compared with control level with normal blood gases an average increase of 13% per 0.05 systemic pH unit decrease. We conclude that systemic CO₂ and H(+) concentrations represent different stimuli to sympathetic nervous system. Despite similar changes of local extracellular pH within rostral ventrolateral medulla during systemic acidosis, different responses of SNA suggest other sites or as yet unknown additional effects of CO₂ as being responsible for excitation of sympathetic activity. Author (Hemer)

A95-74302

ADDUCTOR POLICIS MUSCLE FATIGUE DURING ACUTE AND CHRONIC ALTITUDE EXPOSURE AND RETURN TO SEA LEVEL

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Large muscle exercise performance is impaired during acute exposure to normobaric or hypobaric hypoxia, but the effects of hypoxic conditions on fatigue of isolated smaller muscle groups per se are poorly defined. We studied how acute and chronic altitude (ALT) exposure and post-ALT return to sea level (SL) affects voluntary strength and fatigue of the adductor pollicis muscle. Eight healthy men (mean age 28 yr) were studied on five separate occasions: at SL, on days 1 (acute) and 13 (chronic) at ALT (4,300 m), and on days 1 (post 1) and 3 or 4 (post 2) at SL after 20 days of residence at ALT. On each day, maximal voluntary contractions (MVCs) of the adductor pollicis were obtained before and at the end of each minute of submaximal intermittent contractions of the adductor pollicis (50% of MVC of rested muscle, 5 s of contraction/5 s of rest) until exhaustion, defined as the inability to exert or maintain 50% of rested MVC. MVC of rested muscle did not differ among days. Time to exhaustion was shorter at acute ALT than at SL and tended to be shorter than at chronic ALT. Compared with acute and chronic ALT, time to exhaustion was prolonged during post 1 but not post 2. We conclude that (1) MVC of rested adductor pollicis muscle is not impaired during or after ALT exposure, (2) compared with SL conditions, acute but not chronic ALT exposure leads to a more rapid decline in adductor pollicis MVC associated with submaximal contractions, and (3) time to exhaustion is prolonged for equal to or more than 1 day after return from ALT.

Author (Hemer)

A95-74303

RECOVERY FROM INCREASED PRESSURE OR INCREASED LEAKINESS EDEMA IN PERFUSED SHEEP LUNGS

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Two routes by which interstitial pulmonary edema liquid may leave the lung during recovery are reabsorption into the pulmonary circulation and clearance by lung lymphatics. We hypothesized that reabsorption of edema liquid of low protein concentration into the pulmonary circulation would be greater than reabsorption of edema liquid of high protein concentration because of the greater protein osmotic gradient in the former. On the basis of previous studies, lymph flow should contribute minimally to the recovery. In 22 in situ perfused sheep lungs with lymph fistulas, we produced approximately 100 g of osmotic or hydrostatic edema (low protein) or increased leakiness edema by calcium depletion (high protein). To induce reabsorption, we changed the perfusate from low- (1%

albumin, osmotic pressure = 4 cmH₂O) to high-protein (7% albumin, osmotic pressure = 22 cmH₂O solution in the osmotic group, decreased capillary pressure from 29 +/- 9 to 6 cmH₂O in the hydrostatic group, or reversed leakiness by adding CaCl₂ to the perfusate in the increased leakiness group. Reabsorption occurred only during recovery from osmotic (40 +/- 22% of filtered liquid) and hydrostatic (15 +/- 11%) edema. Total lung lymph flow during recovery from osmotic, hydrostatic, or increased leakiness edema was 4.9 +/- 3.4, 4.3 +/- 3.4, or 3.5 +/- 1.9 g, respectively. We conclude that during recovery from pulmonary edema interstitial liquid is reabsorbed into the circulation in inverse proportion to its protein concentration. We confirm that only a small fraction of the interstitial edema liquid is cleared by the lymphatics during recovery from any type of edema. Author (Hemer)

A95-74304

BIEXPONENTIAL PULMONARY CLEARANCE OF (99 M)-TC-DTPA INDUCED BY DETERGENT AEROSOL

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Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 190-196
Research sponsored by National Association Against Chest and Heart Disease, Swedish Medical Research Council, and AB Procordia Nova
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We measured the pulmonary clearance of technetium-99m-labeled diethylenetriamine pentaacetic acid ((99 m)-Tc-DTPA) for 3 h after perturbation of the surfactant system by administration of the detergent dioctyl sodium sulfosuccinate in aerosol. Forty-two rabbits were anesthetized with pentobarbital sodium. Tracheostomies were performed, and the rabbits were mechanically ventilated. Increasing concentrations of detergent (0.125 - 2%) or vehicle were given for 5 min, and clearance measurements were performed immediately or 60 min after detergent administration. No animals developed respiratory distress. After vehicle, the clearance was monoexponential with a half-life of 153 min. Detergent induced a biexponential clearance with a rapidly clearing additional pool of radioactivity with a half-life of 5 - 15 min. The relative amount of radioactivity clearing rapidly increased with detergent concentration. The detergent effect was partly reversible. We conclude that detergent induces a biexponential clearance of (99 m)-Tc-DTPA by accelerating the transfer of tracer across the alveolocapillary barrier in a proportion of lung units in a dose-related manner.

Author (Hemer)

A95-74305

ELECTROMYOGRAPHIC EVALUATION OF JOINT ANGLE SPECIFICITY AND CROSS-TRAINING AFTER ISOMETRIC TRAINING

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Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 197-201
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The purpose of this study was to examine the effects of unilateral strength training on the strength and integrated electromyogram (IEMG) of the trained and untrained limbs at several joint angles. A training group (TRN; 4 females and 3 males, age 22 +/- 4 yr (SD)) exercised for 6 wk with isometric leg extensions at 80% of maximal isometric torque. A control group (3 females and 3 males, age 24 +/- 4 yr) did not exercise. The training was performed three times per week at 0.79 rad below the horizontal plane. The subjects were tested at joint angles of 0.00, 0.26, 0.79, 1.31, and 1.57 rad. Bipolar surface electrodes were used to record the IEMG of the vastus lateralis. The results indicated a cross-training effect and joint angle specificity for isometric torque in TRN only, with significant increases in torque (collapsed across limb) at 0.26 (23.3%) and 0.79 (22.3%) rad. There was a dissociation, however, between changes in torque and IEMG with an increase in IEMG (collapsed

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across limb and angle) for TRN. The dissociation between the IEMG and strength changes was possibly due to differential responses to training in the four muscles of the quadriceps femoris.

Author (Hemer)

A95-74306

EFFECTS OF ESTRADIOL ON LIPOPROTEIN LIPASE ACTIVITY AND LIPID AVAILABILITY IN EXERCISED MALE RATS

GREGORY S. ELLIS, SUSAN LANZA-JACOBY, ANDREW GOW, and ZEBULON V. KENDRICK *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 209-215 (HTN-95-A0605) Copyright

The effects of 17 beta-estradiol 3-benzoate and exercise on tissue lipid content and lipoprotein lipase (LPL) activity were determined in male rats. Estradiol administration significantly increased fatty acid contents of resting adipose, plasma, and white and red vastus muscle tissues and red vastus muscle triacylglycerol. Adipose and plasma fatty acids and red and white vastus muscle triacylglycerol were significantly higher in exercised estradiol-administered animals than in exercised oil-administered animals. Estradiol administration significantly reduced resting adipocyte LPL activity by 71% and increased myocardial LPL activity by 96%. After exercise, red vastus LPL activity was significantly increased by 76% in estradiol-administered animals compared with oil-administered animals. Ratios of red vastus to adipose LPL activity and myocardial to adipose LPL activity at rest and after exercise were significantly greater in estradiol-administered than in oil-administered animals. Estradiol administration significantly increased the ratio of white vastus to adipose LPL activity of exercised animals. These data indicate that estradiol increases the availability of lipid substrate to exercising muscle from multiple sources, including adipose, plasma, and intracellular muscle triacylglycerol. The absolute increases in muscle LPL activity, combined with a greater ratio of muscle to adipose LPL activity, lead to increased distribution of plasma triacylglycerol-derived fatty acids toward muscle. Author (Hemer)

A95-74307

PHYSIOLOGICAL TOLERANCE TO UNCOMPENSABLE HEAT STRESS: EFFECTS OF EXERCISE INTENSITY, PROTECTIVE CLOTHING, AND CLIMATE

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This study determined the influence of exercise intensity, protective clothing level, and climate on physiological tolerance to uncompensable heat stress. It also compared the relationship between core temperature and the incidence of exhaustion from heat strain for persons wearing protective clothing to previously published data of unclothed persons during uncompensable heat stress. Seven heat-acclimated men attempted 180-min treadmill walks at metabolic rates of approximately 425 and 600 W while wearing full (clo = 1.5) or partial (clo = 1.3) protective clothing in both a desert and tropical climate. During these trials, the evaporation cooling required to maintain thermal balance exceeded the maximal evaporative capacity of the environment and core temperature continued to rise until exhaustion from heat strain occurred. Our findings concerning exhaustion from heat strain are (1) full encapsulation in protective clothing reduces physiological tolerance as core temperature at exhaustion was lower in fully than in partially clothed persons, (2) partial encapsulation results in physiological tolerance similar to that reported for unclothed persons, (3) raising metabolic rate from 400 to 600 W does not alter physiological tolerance when subjects are fully clothed, and (4) physiological tolerance is similar

when subjects are wearing protective clothing in desert and tropical climates having the same wet bulb globe thermometer. These findings can improve occupational safety guidelines for human heat exposure, as they provide further evidence that the incidence of exhaustion from heat strain can be predicted from core temperature.

Author (Hemer)

A95-74308

LACTATE AND ACID-BASE EXCHANGE DURING BRIEF INTENSE CONTRACTIONS OF SKELETAL MUSCLE IN SITU

WILLIAM F. BRECHUE Florida Univ. Health Science Center, Gainesville, FL, US and WENDELL N. STAINSBY Florida Univ. Health Science Center, Gainesville, FL, US *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 223-230 (Contract(s)/Grant(s): NIH-AR-39378) (HTN-95-A0607) Copyright

Our goal was to design a stimulation-contraction paradigm using an isolated in situ dog gastrocnemius muscle preparation that would provide an experimental model for brief intense intermittent (IC) exercise in humans. Second, acid-base and ion exchanges across the muscle were investigated using four 30-s bouts of isotonic tetanic contractions with 4 min of rest between bouts. During the bouts, peak power output (dot-W) was 18.2 m W/g in the first bout; it declined by 4.4% by the fourth bout and by 12 - 16% in each bout. Compared with repetitive continuous contractions (CC) at maximal O₂ uptake (dot-V(sub O₂)), dot-W was greater and dot-V(sub O₂) and CO₂ production were less with IC. Venous-arterial (v-a) differences and lactate output peaked immediately after each bout and were not different from the values reported for CC at maximal dot-V(sub O₂). Thus, with IC, dot-V(sub O₂)/dot-W was lower and the CO₂ production/dot-V(sub O₂) and lactate output/dot-V(sub O₂) ratios were greater than those seen with CC. These difference suggest that this stimulation-contraction paradigm may be an appropriate model for brief intense exercise. The v-a (H⁺) difference was a direct result of the v-a P(sub CO₂) difference. The venous strong ion difference was always greater than or equal to the arterial strong ion difference because the v-a (Cl⁻) difference was opposite and greater than the v-a lactate concentration difference, whereas the v-a (Na⁺) and (K⁺) differences were small. Quantitative estimates for the contribution of active muscle to arterial (H⁺) and lactate concentration during in vivo exercise from the in situ experiments suggest that active muscle does not account completely for the change in either.

Author (Hemer)

A95-74309

NALOXONE DOES NOT AFFECT THE CARDIOVASCULAR AND SYMPATHETIC ADJUSTMENTS TO STATIC EXERCISE IN HUMANS

CHESTER A. RAY Iowa Univ., Iowa City, IA, US and JAMES A. PAWELCZYK Georgia Univ., Athens, GA, US *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 231-235 Research sponsored by Dept. of Veterans Affairs and Presbyterian Hospital of Dallas (Contract(s)/Grant(s): NIH-HL-14388; NIH-HL-24962; NIH-HL-36224) (HTN-95-A0608) Copyright

Previous studies suggested that endogenous opiates may attenuate the cardiovascular and sympathetic adjustments to static exercise. We tested whether this effect originates from exercising skeletal muscles. Eight men performed 2 min of static handgrip (30% maximum) followed by 2 min of posthandgrip muscle ischemia after three interventions: (1) control, (2) intra-arterial injection of naloxone HCl (60 micrograms) or vehicle (saline) in the exercising arm, and (3) systemic infusion of naloxone (4 mg) or vehicle. Naloxone and vehicle trials were performed double blind on separate days. Preexercise baseline muscle sympathetic nerve activity (burst frequency), heart rate, and blood pressure were similar across interventions on either day. During static handgrip, control, intra-arterial, and systemic administration of vehicle and naloxone elicited similar increases in total muscle sympathetic nerve activity and mean arterial pressure. Additionally, there were no differences between vehicle and naloxone trials during posthandgrip muscle ischemia.

Thus, contrary to previous reports, we conclude that the endogenous opiate peptide system does not modulate cardiovascular and sympathetic responses to brief periods of static exercise or muscle ischemia in humans.

Author (Hemer)

A95-74310

EFFECT OF STEP LENGTH OPTIMIZATION ON THE AEROBIC DEMAND OF RUNNING

DON MORGAN, PHILIP MARTIN, MITCH CRAIB, CHRIS CARUSO, ROB CLIFTON, and REGINA HOPEWELL Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 245-251 Research sponsored by Nike, Inc.

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To assess whether distance runners displaying uneconomical freely chosen step lengths (FCSL) could be trained to shift FCSL toward a more optimal setting, six males and three females who exhibited uneconomical FCSL (mean optimal step length (OSL) = -9.81% of leg length from FCSL; mean change in oxygen uptake (dot-V(sub O2)) (FCSL - OSL) = 1.46 ml/kg/min) comprised an experimental group that completed 15 treadmill sessions (30 min/day, 5 days/wk, 3 wk) of OSL training at individually determined running velocities (2.87 - 3.74 m/s). Training sessions featured alternating 5-min periods of combined audio and visual feedback matching OSL and no feedback. A control group of three subjects with uneconomical FCSL (2 males, 1 female) performed 3 wk of treadmill running without feedback. The extent of step length optimization was evaluated by comparing pre- and posttraining differences between FCSL and OSL and between pre- and posttraining dot-V(sub O2). Compared with the control group, the experimental group demonstrated a significantly greater relative shift in FCSL toward OSL and a marked reduction in FCSL dot-V(sub O2). Taken together, these results suggest that short-term audiovisual feedback training can be effective in optimizing step length and producing a decrease in aerobic demand among distance runners exhibiting uneconomical FCSL.

Author (Hemer)

A95-74311

AEROBIC MUSCLE CONTRACTION IMPAIRED BY SEROTONIN-MEDIATED VASOCONSTRICTION

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Vasoconstriction mediated by serotonin (5-HT) inhibits muscle metabolism in resting constant-flow-perfused rat hindlimb and may do so by vascular shunting. In the present study, the effects of 5-HT on tension development and contraction-induced oxygen uptake by the sciatic nerve-stimulated gastrocnemius-plantaris-soleus muscle group of the perfused rat hindlimb and tension development by electrically stimulated isolated incubated soleus and extensor digitorum longus muscles were examined. In both erythrocyte and erythrocyte-free perfusions, 0.25 micrometer 5-HT increased perfusion pressure and markedly decreased contraction-induced tension, oxygen uptake, and lactate release. The release of metabolic vasodilators from exercising skeletal muscle did not appear to affect 5-HT-mediated vasoconstriction; rather, vascular resistance increased during the period of muscle contraction. In contrast, vasoconstriction during muscle contraction mediated by alpha-adrenoceptor stimulation did not impair tension and was partially overcome by metabolic vasodilators. In addition, contraction of isolated incubated soleus and extensor digitorum longus muscles was not affected by 5-HT addition to the incubation medium. We conclude that 5-HT impairs contractility of working muscle during the aerobic phase by limiting oxygen delivery through redistributing perfusate flow. The results are consistent with a vasoconstrictor action of 5-HT on larger vessels, perhaps at feed arteries external to the working muscle. When constricted by 5-HT, these

vessels are apparently insensitive to metabolic vasodilatation.

Author (Hemer)

A95-74312

EFFECT OF DOPAMINE ON HYPOXIC VENTILATORY RESPONSE OF SEDATED PIGLETS WITH INTACT AND DENERVATED CAROTID BODIES

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To determine whether the neonatal hypoxic ventilatory depression is in part produced by an increased endogenous dopamine release that can depress the activity of central and peripheral chemoreceptors, 31 sedated and spontaneously breathing newborn piglets were randomly assigned to an intact carotid body or a chemodenervated group. Minute ventilation (dot-VE), arterial blood pressure, and cardiac output (CO) were measured in room air before infusion of saline or the dopamine antagonist flupentixol (0.2 mg/kg iv) and 15 min after drug infusion and were repeated after 10 min of hypoxia (inspiratory O2 fraction = 0.10). Dot-VE increased significantly after 10 min of hypoxia in the piglets that received flupentixol independent of whether the carotid bodies were intact or denervated. However, the increase in dot-VE was largest and sustained throughout the 10 min of hypoxia only in the intact carotid body flupentixol group. As expected, the initial increase in dot-VE with hypoxia was abolished by carotid body denervation. Changes in arterial blood gases, CO, and mean arterial blood pressure with hypoxia were not different among groups. These results demonstrate that flupentixol reverses the late hypoxic decrease in dot-VE, acting through peripheral and central dopamine receptors. This effect is not related to changes in cardiovascular function or acid-base status.

Author (Hemer)

A95-74313

DIFFERENTIAL RESPONSE OF MACROPHAGE SUBPOPULATIONS TO SOLEUS MUSCLE RELOADING AFTER RAT HINDLIMB SUSPENSION

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The hypothesis that distinct populations of macrophages are associated with muscle necrosis and regeneration were examined in Wistar rat soleus muscle after 10 days of hindlimb suspension and 2, 4, and 7 days after the resumption of weight bearing. Necrosis was identified using histological features, such as muscle fiber in filtration, and regeneration was identified using immunohistochemical techniques for developmental myosin heavy chain (dMHC). Light-microscopic observations show that necrotic fibers in 2-day reloaded soleus muscle were invaded by ED1(+) and Ia(+) macrophages. The number of invaded fibers in muscles reloaded for 2 days increased to 2.8/sq mm compared with 0.2/sq mm in age-matched normal muscle but returned to control values by the 4th day of resumed weight bearing. In the interstitial spaces of 2-day recovery muscle, ED1(+) and Ia(+) macrophages numbered 369 and 332/sq mm, respectively, compared with 12 and 72/sq mm, respectively, in control soleus. After 7 days of reloading, the number of ED1(+) cells was similar to that of control. Ia(+) macrophages decreased to 240/sq mm at 4 days but after 7 days rose above control values to 429/sq mm. ED2(+) macrophages in 4- and 7-day reloaded soleus increased 70 - 80% in the interstitial spaces compared with control but were not observed to infiltrate necrotic muscle fibers at any time points. Immunohistochemistry and immunoblots using a monoclonal anti-dMHC antibody demonstrate a greater proportion of myofibers expressing dMHC isoforms after 4

and 7 days of reloading. These findings indicate that macrophage subpopulations are associated with distinct stages during the recovery process from hindlimb suspension: ED1(+) macrophages are associated with muscle necrosis, whereas ED2(+) cells are associated with muscle regeneration. Data from this investigation also suggest that Ia(+) macrophages may respond to both muscle injury response stages.

Author (Herner)

A95-74314

EFFECTS OF TRAINING ON BLOOD LACTATE-RUNNING SPEED RELATIONSHIP IN THOROUGHBRED RACEHORSES

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In this study the effects of training history on the results of a standardized two-speed test in competing Thoroughbreds were investigated during a racing season. For nine Thoroughbreds, 1,755 training days were recorded. Within the observation period each horse completed a two-speed field test at intervals of 6 - 8 wk to determine its running velocity (V) eliciting blood lactate concentrations of 4 (V(sub 4)) and 12 mmol/l (V(sub 12)). Horses performed 29 two-speed tests. Changes of V(sub 4) and V(sub 12) in a horse between two consecutive tests were used to assess effects of training history variables calculated for the period between two consecutive tests. The percentage of days with gallop workouts between two consecutive tests showed a significant correlation with changes in V(sub 4) and V(sub 12). The number of gallop workouts and the total time of training correlated with the change of V(sub 4). Furthermore the percentage of days without training was negatively correlated to changes of V(sub 4) and V(sub 12). Therefore the actual training caused changes in the blood lactate-running speed relationship despite its relatively low volume, intensity, and frequency. Future studies have to evaluate how the training variables can be changed to improve the training effects on the blood lactate-running speed relationship of competing Thoroughbreds.

Author (Herner)

A95-74315

EFFECT OF LIPID ON INERT GAS KINETICS

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A Monte Carlo simulation of inert gas transit through skeletal muscle has been extended to include regions of increased gas solubility to simulate regions of high lipid content. Position of the regions within the simulation module was varied, as was the muscle-lipid partition coefficient (lambda). The volume percentage of the lipid regions (alpha) was varied from 1 to 25% while lambda covered the range from 1 to 50. The effects of alpha and lambda on mean transit time and on relative dispersion (RD; ratio of SD to the mean) were examined for a single lipid volume and compared with expected values under the assumption that the tissue is composed of two well-stirred compartments. Mean transit times varied from approximately 0.80 to 1.20 times the values predicted by a simple parallel two-compartment model, whereas RD varied from 0.9 to 3.6. For fixed lambda, RD as a function of lipid fraction passes through a maximum that is shifted and was also smaller than expected from a simple two-compartment model. For fixed alpha, RD approaches an asymptotic value for large lambda, but the asymptote is smaller than that expected from the two-compartment model. When lipid is distributed in only two regions, RD decreases with increasing separation of the regions and with increasing surface area of the fat regions. A model of two well-stirred compartments that allows mixing between the compartments yields results similar to those from the simulation.

Author (Herner)

A95-74316

TIME COURSE OF AUGMENTATION AND DEPRESSION OF HYPOXIC VENTILATORY RESPONSES AT ALTITUDE

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Hypoxic ventilatory response (HVR) and hypoxic ventilatory depression (HVD) were measured in six subjects before, during, and after 12 days at 3,810-m altitude (barometric pressure approximately 488 Torr) with and without 15 min of preoxygenation. HVR was tested by 5-min isocapnic steps to 75% arterial O₂ saturation measured by pulse oximetry (Sp(sub O₂)) at an isocapnic PCO₂ (P*CO₂) chosen to set hyperoxic resting ventilation to 140 ml/kg/min. Hypercapnic ventilatory response was tested at ambient and high Sp(sub O₂) 6 - 8 min after a 6- to 10-Torr step increase of end-tidal PCO₂ above P*CO₂. HCVR was independent of preoxygenation and was not significantly increased at altitude. Preoxygenated HVR rose from -1.13 +/- 0.23 (SE) l/min/% Sp(sub O₂) at sea level to -2.17 +/- 0.13 by altitude day 12, without reaching a plateau, and returned to control after return to sea level for 4 days. Ambient HVR was measured at P*CO₂ by step reduction of Sp(sub O₂) from its ambient value (86 - 91%) to approximately 75%. Ambient HVR slope was not significantly less, but ventilation at equal levels of Sp(sub O₂) and PCO₂ was lower by 13.3 +/- 2.4 l/min on day 2 and by 5.9 +/- 3.5 l/min on day 12. This lower ventilation was estimated (from HCVR) to be equivalent to an elevation of the central chemoreceptor PCO₂ set point of 9.2 +/- 2.1 Torr on day 2 and 4.5 +/- 1.3 on day 12. We conclude that, at 3,810 m, (1) hypoxic chemosensitivity doubles over 12 days and (2) HVD is manifest not as a lower HVR slope but as a lower ventilation, as if the central chemoreceptor ventilatory PCO₂ set point were increased.

Author (Herner)

A95-74317

N-ACETYLCYSTEINE DEPRESSES CONTRACTILE FUNCTION AND INHIBITS FATIGUE OF DIAPHRAGM IN VITRO

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We have previously shown that antioxidant enzymes (superoxide dismutase and catalase) depress contractility of unfatigued diaphragm fiber bundles and inhibit development of acute fatigue. In the present study, we tested for similar effects of N-acetylcysteine (NAC), a nonspecific antioxidant approved for clinical use. Diaphragms were excised from deeply anesthetized rats. Fiber bundles were removed, mounted isometrically at 37 C, and stimulated directly using supramaximal current intensity. Studies of unfatigued muscle showed that 10 mM NAC reduced peak twitch stress, shortened time to peak twitch stress, and shifted the stress-frequency curve down and to the right. Fiber bundles incubated in 0.1 - 10 mM NAC exhibited a dose-dependent decrease in relative stresses developed during 30-Hz contraction with no change in maximal tetanic (200 Hz) stress. NAC (10 mM) also inhibited acute fatigue. Throughout 10 min of intermittent contraction at 30 - 40 Hz, treated bundles developed higher stresses than time-matched control bundles. NAC concentrations equal to or greater than 30 mM were toxic, causing a prompt irreversible decrease in maximal tetanic stress. Because NAC effects mimic the effects of other antioxidant agents with different mechanism of action, we conclude that exogenous antioxidants exert stereotypical effects on contractile function that differ between unfatigued and fatiguing muscle. Unlike antioxidant enzymes, however, NAC has been approved for clinical use and may be used in future studies of human muscle fatigue.

Author (Herner)

A95-74318

ISOPROTERENOL DECREASES PROTEIN PERMEABILITY IN EDEMATOUS ISOLATED RABBIT LUNGS: ESTIMATION OF PS AND SIGMA

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The objective of the present study was to determine whether the ability of the beta-adrenergic agonist isoproterenol to attenuate pulmonary edema occurs via a permeability and/or hemodynamic mechanism. In isolated perfused rabbit lungs, the resistive property of the vascular barrier to the movement of fluid and protein was assessed by measurements of the capillary filtration coefficient ($K_{\text{sub f}}$) and the transvascular clearance of I-125-labeled albumin, respectively. Regression analysis of albumin clearance vs. transvascular fluid flux was performed to estimate the permeability-surface area product (PS) and the reflection coefficient (sigma) by use of the linear or nonlinear flux equation. Arterial, capillary, and venous pressures and resistances, weight gain, and the wet-to-dry weight ratio were also assessed. Isoproterenol attenuated the arachidonic acid (4 mg)-induced increases in fluid flux, wet-to-dry weight ratio, albumin clearance, and PS and the decrease in sigma. Isoproterenol had no effect on the increase in $K_{\text{sub f}}$, and there was no correlation between capillary pressure and fluid flux in any of the four groups. Regression analysis revealed that the nonlinear flux equation provided estimates of PS and sigma that more accurately described the statistical differences in albumin clearance among the groups studied than the linear flux equation. These findings demonstrate that isoproterenol attenuated the increased transvascular flux of albumin in edematous lungs by modifying the protein permeability of the vascular barrier.

Author (Herner)

A95-74319

PULMONARY CAPILLARY TRANSPORT FUNCTION FROM FLOW-LIMITED INDICATORS

SAID H. AUDI, GARY S. KRENZ, JOHN H. LINEHAN, DAVID A. RICKABY, and CHRISTOPHER A. DAWSON *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 332-351 (Contract(s)/Grant(s): NIH-HL-24349) (HTN-95-A0618) Copyright

The objective of this study was to examine the use of rapidly diffusing (flow-limited) indicators for estimating the pulmonary capillary blood volume (i.e., fraction of the lung blood volume wherein the diffusible indicators equilibrate with the tissue) and the capillary transit time distribution. Supporting theory and an application to experimental data are presented. The theory leads to equations, which relate the mean transit time, the variance, and the third central moment of the capillary transport function, to the moment of the venous concentration-time curves for a vascular reference indicator, and a flow-limited diffusible indicator after a bolus injection of the indicators upstream from an organ. The moments of $h(\text{sub c})t$ can be estimated if the injected bolus includes, along with the vascular reference indicator, at least two flow-limited diffusible indicators, each with a different $\text{bar-t}(\text{sub e})$. A least-squares optimization procedure can then be used to specify the moments of $h(\text{sub c})t$. This approach was applied to isolated dog lung lobes with C-14 diazepam as the diffusible indicator. The tissue-to-perfusate partition coefficient for C-14 diazepam could be adjusted to any desired value by altering the perfusate albumin concentration. Thus, by making a number of injections, each at a different perfusate albumin concentration, data were obtained in a manner equivalent to making one injection with a number of flow-limited diffusible indicators, each with a different $\text{bar-t}(\text{sub e})$. On average, the estimated

capillary volume and mean transit time were approximately 48% of the total lobar volume and mean transit time, and the relative dispersion of the $h(\text{sub c})t$ was approximately 75%.

Author (Herner)

A95-74320

TRACHEAL MUCOSAL EDEMA IN HYDROSTATIC PULMONARY EDEMA

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Airway edema has been described in heart failure, and, in animal experiments, airway narrowing was observed with elevated left arterial pressure (Pla). On the basis of double-indicator-dilution principles using helium and dimethylether, we were able to measure a water compartment of the tracheal mucosa ($V(\text{sub H}_2\text{O})$) in dogs. Hypervolemia with an attendant increase in Pla caused by infusion of 2 liters of dextran increased $V(\text{sub H}_2\text{O})$ from 368 ± 71 (SE) to 794 ± 177 microliters. Pulmonary arterial wedge and central venous pressures ($P(\text{sub CV})$) rose concomitantly. Increases in pulmonary arterial wedge and $P(\text{sub CV})$ by a left atrial balloon catheter produced similar increases in $V(\text{sub H}_2\text{O})$, whereas increases in $P(\text{sub CV})$ alone by a right atrial balloon did not increase $V(\text{sub H}_2\text{O})$. Increasing $V(\text{sub H}_2\text{O})$ by dextran infusion was associated with an increase in pulmonary resistance from 1.16 ± 0.19 to 2.15 ± 0.24 $\text{cmH}_2\text{O/l/s}$. These observations show that fluid accumulation in the lung during pulmonary congestion also involves extraparenchymal airways and is related to Pla rather than right atrial pressure. This indicates that sufficient collateral drainage exists during right-sided but not left-sided pressure elevations.

Author (Herner)

A95-74321

EFFECTS OF INCREASED ENERGY INTAKE AND/OR PHYSICAL ACTIVITY ON ENERGY EXPENDITURE IN YOUNG HEALTHY MEN

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This study was designed to examine effects of alterations in energy balance on adaptive changes in components of total energy expenditure (TEE). Nineteen young healthy males were studied during a 10-day sedentary energy balance baseline period and then randomly assigned to one of four 10-day treatment groups: (1) no change in energy intake (EI) or physical activity (PA); energy balance at low energy flux, (2) EI increased by 50% with no change in PA (positive energy balance), (3) TEE increased by 50% by increasing PA, matched by a 50% increase in EI (energy balance at high energy flux), and (4) TEE increased by 50% by increasing PA with no change in EI (negative energy balance). TEE was measured with doubly labeled water, resting metabolic rate (RMR) by indirect calorimetry, and thermic response to feeding (TEF) by indirect calorimetry; energy expenditure of physical activity (EEPA) was estimated by subtracting RMR, TEF, and prescribed PA from TEE. TEE was significantly increased by PA (by design) but not EI. There was a significant main effect of intake and a significant intake-by-activity interaction for changes in RMR. In post hoc analysis, RMR was significantly increased during positive energy balance and energy balance at high energy flux relative to change in RMR when

energy balance was maintained at low energy flux. A significant increase in RMR was also noted during negative energy balance after adjustment for change in fat-free mass. There was no significant difference in change in RMR among the three treatment groups. There was no significant main effects of intake or activity on EEPA or thermic effect of a meal. These results suggest that in young healthy males living under tightly controlled conditions (1) adaptive changes in TEE in response to short-term alterations in energy balance are mediated primarily through changes in RMR, (2) RMR can be elevated during a state of energy balance when energy flux is increased, and (3) magnitude of adaptive change in RMR is similar in response to increased EI and/or PA; therefore simultaneous increases in energy intake and physical activity do not act synergistically to raise RMR. Author (Hemer)

A95-74322

**AIRWAY AND TISSUE MECHANICS DURING
PHYSIOLOGICAL BREATHING AND
BRONCHOCONSTRICTION IN DOGS**

KENNETH R. LUTCHEN, BELA SUKI, QIN ZHANG, FERENC PETAK, BALINT DAROCZY, and ZOLTAN HANTOS *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 373-385 Research sponsored by Hungarian Basic Research Fund (Contract(s)/Grant(s): NSF BCS-93-09426) (HTN-95-A0621) Copyright

In five open-chest dogs and with four to five alveolar capsules we used an optimal ventilator waveform (OVW) to follow frequency and tidal volume ($V_{\text{sub T}}$) dependence of lung, airway, and tissue resistance (R) and elastance (E) before and during constant infusion of histamine. OVW contains sufficient flow energy between 0.234 and 4.7 Hz, avoids nonlinear harmonic interactions, and simultaneously ventilates with physiological $V_{\text{sub T}}$. Each OVW breath permits a smooth estimate of frequency dependence of R and E for the whole lung. A constant-phase model analysis provided estimates of purely viscous resistance (R_{vis}), which represents the sum of airway resistance (R_{aw}) and any purely newtonian component of tissue resistance (R_{ti}), and parameters G and H, which govern frequency dependence of R_{ti} and tissue elastance (E_{ti}), respectively. Tissue structural damping (η) is calculated as G/H . This model was applied to the whole lung and tissue impedance as estimated from each capsule. We found a small but inconsequential purely newtonian component of R_{ti} , even during constriction. Four dogs showed a peak response at approximately 4 min in lung R_{vis} coupled (in time) to initial increases in G, H, η , and airway inhomogeneities. In two of these dogs the response was severe. Tissue properties estimated from whole lung impedance (G, H, and η) were nearly identical to values estimated from unobstructed capsules throughout infusion. By using a technique independent of alveolar capsules, our results indicate that a major if not dominant response to a constrictive agonist occurs in lung tissues, resulting in a large increase in R_{ti} and E_{ti} . With severe constriction, significant increases occur in R_{ti} and airway inhomogeneities as well. Finally, separation of airway and tissue properties using input impedance estimated from the frequency-rich OVW avoids use of alveolar capsules and may prove an effective tool for partitioning airway and tissue properties in humans. Author (Hemer)

A95-74323

**PULMONARY ARTERIAL SMOOTH MUSCLE CONTRACTILITY
IN HYPOXIA-INDUCED PULMONARY HYPERTENSION**

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The highly compliant low-resistance pulmonary vasculature is markedly altered with chronic hypoxia. Remodeling in response to hypoxia and/or hypertension involves hypertrophy and hyperplasia

of smooth muscle and excessive deposition of connective tissue that likely contributes to the maintenance or exacerbates the already elevated pulmonary arterial (PA) pressure. The purpose of this study was to investigate the effect of chronic hypoxia on the contractile properties of PA smooth muscle. Isometric and isotonic experiments were performed on excised PA rings from pulmonary hypertensive (induced by 14 days of hypoxia) Sprague-Dawley rats. A doubling of the vessel wall thickness occurred during the development of hypoxia-induced pulmonary hypertension. Functionally, there was a decrease in isometric stress (force to cross-sectional area ratio). No difference was detected in the velocity of shortening or in total shortening ability. This study provides evidence that, in addition to the morphological changes, changes in PA smooth muscle contractility also appear to play a role in the development and/or maintenance of hypoxia-induced pulmonary hypertension. Author (Hemer)

A95-74324

**RELATIONSHIPS BETWEEN ENERGY EXPENDITURE AND
POSITIVE AND NEGATIVE MECHANICAL WORK IN
REPETITIVE LIFTING AND LOWERING**

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Determining the separate energy costs of the positive and negative mechanical work in repetitive lifting or lowering is quite complex, as a mixture of both work components will always be involved in the up- and downward motion of the lifter's body mass. In the current study, a new method was tested in which coefficients specifically related to the positive and negative work were estimated by multiple regression on a data set of weight-lifting and weight-lowering tasks. The energy cost was obtained from oxygen uptake measurements. The slopes of the regression lines for energy cost and mechanical work were steeper for positive than for negative work. The cost related to the negative work was approximately 0.3 - 0.5 times the cost of the positive work. This finding is well in line with data obtained directly from other isolated activities of either positive or negative work (e.g., ladder climbing vs. descending). However, the intercept values of the regression lines were not significantly different from zero or were even negative. This was most likely due to the metabolic energy not related to processes that yield mechanical work (e.g., isometric muscle actions) that was not constant among trials. Author (Hemer)

A95-74325

**ROLE OF SEX HORMONES IN DEVELOPMENT OF CHRONIC
MOUNTAIN SICKNESS IN RATS**

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After chronic exposure to hypoxia, Hilltop Sprague-Dawley rats developed excessive polycythemia and severe pulmonary hypertension and right ventricular (RV) hypertrophy, signs consistent with human chronic mountain sickness; however there were gender differences in the magnitude of the polycythemia and susceptibility to the fatal consequence of chronic mountain sickness. Orchiectomy and ovariectomy were performed to evaluate the role of sex hormones in the gender differences in these hypoxic responses. After 40 days of exposure to simulated high altitude, both sham-gonadectomized male and female rats developed polycythemia and had increased RV peak systolic pressure and RV hypertrophy. The hematocrit was slightly but significantly higher in males than in

females. Orchiectomy did not affect these hypoxic responses, although total ventricular weight was less in the castrated high-altitude rats. At high altitude, the mortality rates were 67% in the sham-operated male rats and 50% in the castrated animals. In contrast, ovariectomy aggravated the high-altitude-associated polycythemia and increased RV peak systolic pressure and RV weight compared with the sham-operated high-altitude female rats. Both sham-operated control and ovariectomized females suffered negligible mortality at high altitude. The present study demonstrated that (1) the male sex hormones play no role in the development of the excessive polycythemia, pulmonary hypertension, and RV hypertrophy during chronic hypoxic exposure or in the associated high mortality and (2) the female sex hormones suppressed both the polycythemic and cardiopulmonary responses in vivo during chronic hypoxic exposure. Author (Hemer)

A95-74326

CARDIORESPIRATORY CHANGES DURING MICROWAVE-INDUCED LETHAL HEAT STRESS AND BETA-ADRENERGIC BLOCKADE

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Ketamine-anesthetized Sprague-Dawley rats were exposed to 2,450-MHz microwaves at an average power density of 60 m W/sq cm until lethal temperatures were attained. The effects of propranolol, nadolo, and labetalol on physiological responses (including changes in body temperature, heart rate, blood pressure, and respiratory rate) were examined. Lethal temperatures in the labetalol and both propranolol groups were significantly lower than in saline controls. Survival time was significantly less only in the high-dose propranolol group. In all groups, heart rate increased continuously during exposure; blood pressure increased until colonic temperature reached 41-41.5°C and then decreased. These heart rate and blood pressure changes were similar to those that occur during environmental heat stress. Heart rate and blood pressure changes among groups were similar. Respiratory rate, however, was significantly elevated during most of the exposure period in the high-dose propranolol animals. This change in respiration, coupled with the significantly lower survival time in these animals, suggests a vital role of respiration in susceptibility to microwave-induced heating. Author (Hemer)

A95-74327

AIRWAY GEOMETRY AND WALL MECHANICAL PROPERTIES ESTIMATED FROM SUBGLOTTAL INPUT IMPEDANCE IN HUMANS

ROBERT H. HABIB, RICHARD B. CHALKER, BELA SUKI, and ANDREW C. JACKSON Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 441-451 Research sponsored by Whitaker Foundation (Contract(s)/Grant(s): NIH-HL-31248) (HTN-95-A0626) Copyright

We measured input impedance between 16 and 2,048 Hz intubated subjects at functional residual capacity. The corresponding subglottal impedances ($Z(\text{sub SG})$) were then computed using a model where the endotracheal tube was represented by a distributed-parameter two-port network. $Z(\text{sub SG})$ was well described by a model based on Horsfield's asymmetric airway geometry at total lung capacity (TLC) with nonrigid walls. The walls of the cartilaginous airways included separate cartilage and soft tissue compartments, whereas the noncartilaginous airway walls had only a soft tissue compartment. Both compartments consisted of a series resistance, inductance, and compliance, the values of which were computed from airway dimensions and wall material properties (viscosity, density, and Young's modulus). Airway wall thickness was determined by scaling an airway wall area-diameter relationship. Airway lengths and diameters were scaled from the Horsfield TLC values by a single factor and by an order-dependent sigmoidal curve, respectively. The estimated soft tissue viscosity and Young's

modulus were 1.04 ± 0.21 cmH₂O/s and 593 ± 319 cmH₂O respectively. Airway lengths and tracheal diameters were not statistically different from the Horsfield values. The estimated diameters of the more peripheral airways were significantly reduced compared with the Horsfield TLC values, which is consistent with the reduction in airway caliber when the lung deflates from TLC to functional residual capacity. These results indicate that high-frequency $Z(\text{sub SG})$ is sensitive to subglottal airway geometry and wall properties and that by use of appropriate structural models one can estimate airway geometry and airway wall parameters. Author (Hemer)

A95-74328

EFFECT OF HELIUM-INDUCED VENTILATORY UNLOADING ON BREATHING AND DIAPHRAGM EMG IN AWAKE PONIES

H. V. FORSTER, B. K. ERICKSON, T. F. LOWRY, L. G. PAN, M. J. KORDUCKI, and A. L. FORSTER Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 452-462 Research sponsored by Veterans Affairs (Contract(s)/Grant(s): NIH-HL-25739) (HTN-95-A0627) Copyright

Two questions were addressed in this study: (1) Does respiratory resistive unloading (inspired O₂ fraction = 0.21, inspired He fraction = 0.79) elicit a compensatory reduction in stimulation of the diaphragm? (2) Do diaphragm and lung afferents contribute to compensatory responses to unloading? Ten intact (I), five diaphragm-deafferented (DD), four hilar nerve-denervated (HND), and seven DD + HND adult ponies were studied at rest and during mild and moderate treadmill exercise. During steady-state unloading at rest, duration of the diaphragm electromyogram (EMG (sub di)) was less than control in I ponies, but there were no additional significant changes in breathing or blood gases. Unloading during mild and moderate exercise increased pulmonary ventilation in all groups, and this response did not differ among the groups. With unloading during exercise, arterial P(sub CO₂) was within 1 Torr of control except in the DD + HND ponies, which were 1-2 Torr hypocapnic. During exercise, the duration and rate of the EMG(sub di) were reduced below control, beginning at about the third unloaded breath. The decrease in rate of rise was usually not sustained, inasmuch as there was a gradual return toward control over 2 min of unloading. There were no consistent group differences in these EMG(sub di) responses. We conclude that resistive unloading during mild and moderate exercise in ponies results in a transient reduction in neural drive to the diaphragm that is not critically dependent on diaphragm and pulmonary afferents. Author (Hemer)

A95-74329

CONTRIBUTIONS OF CAPILLARY PATHWAY SIZE AND NEUTROPHIL DEFORMABILITY TO NEUTROPHIL TRANSIT THROUGH RABBIT LUNGS

BARRY R. WIGGS, DEAN ENGLISH, WILLIAM M. QUINLAN, NICHOLAS A. DOYLE, JAMES C. HOGG, and CLAIRE M. DOERSCHUK Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994 p. 463-470 Research sponsored by Medical Research Council of Canada and American Lung Association (Contract(s)/Grant(s): NIH-HL-48160) (HTN-95-A0628) Copyright

Neutrophil margination within the pulmonary capillary is due to a delay in their transit compared with that of red blood cells (RBC). This delay has been attributed to the large fraction of capillary segments that are narrower than spherical neutrophils and differences between the time required for deformation of neutrophils and that required for deformation of RBC. This study investigated the characteristics of neutrophil deformation in vivo and the perfusion patterns of segments within capillary pathways. Studies comparing the extraction of neutrophils with that of nondeformable microspheres in one transit through the pulmonary circulation suggest that neutrophils can undergo a rapid deformation from 6.4 to 5.0-5.1 micrometers, whereas larger deformations require a delay. Effective diameters of the perfused capillary pathways were larger than expected for a random distribution of capillary segment diameters within these

pathways. The longer transit times of neutrophils in the upper regions of the lung were associated with a greater fraction of pathways containing narrow segments. These studies suggest that neutrophil deformability and capillary pathway diameters are important in determining the size of the margined pool of neutrophils within the pulmonary capillaries. Author (Hemer)

A95-74330

STIMULUS-RESPONSE CURVE OF HYPOXIC PULMONARY VASOCONSTRICTION IN INTACT DOGS: EFFECTS OF ASA

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Hypoxic pulmonary vasoconstriction (HPV) has been reported to decrease during severe hypoxia in isolated lungs, but it remains unknown whether this decrease occurs in the intact animal and how it is affected by cyclooxygenase inhibition. We investigated the HPV stimulus-response relationship in eight pentobarbital sodium-anesthetized intact dogs with a naturally occurring response to hypoxia ('responders'). The pulmonary arterial minus wedge pressure difference (Ppa - Ppw) was measured at 11 inspired O₂ fraction (FI(sub O₂)) values between 0.40 and 0.04 while ventilation, cardiac output, and acid-base status were kept constant. Ppa - Ppw increased by 8 +/- 1 mmHg between FI(sub O₂) of 0.40 and 0.10 and decreased by 3 +/- 1 mmHg between FI(sub O₂) of 0.10 and 0.04. To assess the effects of cyclooxygenase inhibition, similar stimulus-response curves were obtained after administration of 20 mg/kg of acetylsalicylic acid (ASA) in 16 more dogs selected as either nonresponders or responders to hypoxia. ASA restored HPV in nonresponders and enhanced HPV in responders, with the difference between Ppa - Ppw at FI(sub O₂) of 0.10 and 0.40 increasing from 1 +/- to 8 +/- 1 mmHg and from 7 +/- to 10 +/- 1 mmHg, respectively. In both groups, the shape of the stimulus-response curve after ASA was comparable to that of spontaneous HPV, with a maximum at FI(sub O₂) of 0.10 and a significant decrease at lower FI(sub O₂). We conclude that severe hypoxia attenuates HPV in the intact animal and that ASA restores or enhances HPV by affecting the magnitude of the hypoxic response and not the sensitivity to hypoxia.

Author (Hemer)

A95-74331

CONTRACTILE PROPERTIES OF THE DEVELOPING DIAPHRAGM CORRELATE WITH MYOSIN HEAVY CHAIN PHENOTYPE

B. D. JOHNSON, L. E. WILSON, W. Z. ZHAN, J. F. WATCHKO, M. J. DAOOD, and G. C. SIECK Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 1 July 1994

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The objective of this study was to determine the relationship between developmental transitions in myosin heavy chain (MHC) composition and changes in maximum unloaded shortening velocity (V(sub o)) and maximum specific force (P(sub o)) of the rat diaphragm muscle. The diaphragm was excised at postnatal days 0, 3, 7, 14, 21, and 28 and in adults. MHC isoform expression was determined by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and laser densitometry. In muscle fiber bundles, V(sub o) was determined at 15 C by use of the 'slack' test. Isometric P(sub o) was determined at 15 and 26 C. Simple and step-wise regressions were used to evaluate the correlations between V(sub o), P(sub o), and MHC phenotype transitions and the various developmental ages. The progressive increases in V(sub o) and P(sub o) with age

were found to be inversely correlated to MHC-neonatal isoform expression and positively correlated to MHC-2X and MHC-2B isoform expression. Changes in MHC-neonatal isoform expression contributed to most of the developmental variance in V(sub o) and P(sub o), with changes in MHC-2X and MHC-2B expression also contributing significant increments to total variance. The postnatal increase in V(sub o) most likely relates to differences in the actomyosin adenosinetriphosphatase activity between neonatal and adult fast MHC phenotypes. The increase in P(sub o) may reflect inherent differences in myofibrillar density, cross-bridge cycling kinetics, and/or the force produced per cross-bridge among fibers composed of the different MHC isoforms. Author (Hemer)

A95-74332

PROLONGED PULMONARY VASCULAR HYPERREACTIVITY IN CONSCIOUS DOGS AFTER CARDIOPULMONARY BYPASS

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Although cardiopulmonary bypass (CPB) is required in all surgical procedures involving open-heart surgery, the extent to which CPB alters pulmonary vascular regulation has not been systematically investigated. Our objectives were to investigate the acute, subacute, and chronic effects of CPB on the left pulmonary vascular pressure-flow (LP-dot-Q) relationship in conscious dogs. Continuous LP-dot-Q plots were generated in chronically instrumented conscious dogs 2 - 4 days pre-CPB and again 4 h and 1, 2, 7, and 14 days after 2.5 h of closed-chest hypothermic CPB. In addition, pulmonary vascular reactivity was assessed by examining the dose-response relationship to the thromboxane analogue U-46619 pre- and post-CPB. CPB resulted in an acute (4 h post-CPB) shift in the baseline LP-dot-Q relationship, indicating an increase in pulmonary vascular resistance. The baseline LP-dot-Q relationship returned to pre-CPB values by 1 day post-CPB. Despite this return of the baseline LP-dot-Q relationship to pre-CPB values, the pulmonary vasoconstrictor response to U-46619 was markedly potentiated 2 days post-CPB compared with the pre-CPB response. This enhanced pulmonary vasoconstrictor response to U-46619 was still apparent 7 days post-CPB but was not evident 14 days post-CPB. These results indicate that CPB results in a pronounced, but transient, increase in pulmonary vascular resistance. Moreover, CPB causes a protracted increase in pulmonary vascular reactivity even when the baseline LP-dot-Q relationship has returned to pre-CPB values. This experimental model can be used to assess the specific effects of CPB on acute and chronic mechanisms of pulmonary vascular regulation. Author (Hemer)

A95-74333

EFFECTS OF A CHRONIC AORTOPULMONARY SHUNT ON PULMONARY HEMODYNAMICS IN PIGLETS

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Systemic-to-pulmonary shunting in growing pigs has been proposed as an experimental model of high-flow pulmonary hypertension associated with congenital heart defects. We investigated multipoint pulmonary arterial pressure (Ppa) vs. cardiac output (dot-Q) plots and pulmonary vascular impedance spectra in 13 piglets

aged approximately 4 mo and ventilated alternately in hyperoxia and in hypoxia. The measurements were done 8 wk after either an anastomosis between the thoracic aorta and the pulmonary trunk or a sham operation. Cardiac output was altered by a manipulation of venous return. In the sham-operated piglets, hypoxia increased Ppa by an average of 12 mmHg over the entire range of dot-Q studied, from 60 to 120 ml/kg, and increased both \dot{O}_2 ($Z(\text{sub } 0)$) and characteristic (Z_c) pulmonary vascular impedance. In the shunted piglets compared with the sham-operated piglets in hyperoxia, Ppa was increased by an average of 5 - 6 mmHg at all levels of dot-Q studied, from 60 to 120 ml/kg, and Z_c was also increased, whereas $Z(\text{sub } 0)$ was unchanged. In the shunted piglets, hypoxia increased Ppa at all levels of dot-Q studied only to an average of 3 mmHg, and neither $Z(\text{sub } 0)$ nor Z_c was altered by hypoxia. We conclude that an aortopulmonary shunt of 2-mo duration in growing pigs increases both pulmonary vascular resistance and impedance and is associated with a blunting of pulmonary vascular reactivity to hypoxia.

Author (Hemer)

A95-74334

ADDITIVE EFFECT OF CONTRACTIONS AND INSULIN ON GLUT-4 TRANSLLOCATION INTO THE SARCOLEMMMA

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The maximal effects of insulin and muscle contractions on glucose transport are additive. GLUT-4 is the major glucose transporter isoform expressed in skeletal muscle. Muscle contraction and insulin each induce translocation of GLUT-4 from intracellular sites into the plasma membrane. The purpose of this study was to test the hypothesis that the incremental effect of contractions and insulin on glucose transport is mediated by additivity of the maximal effects of these stimuli on GLUT-4 translocation into the sarcolemma. Anesthetized rats were given insulin by intravenous infusion to raise plasma insulin to 2,635 \pm 638 microunits/ml. The gastrocnemius-plantaris-soleus group was stimulated to contract via the sciatic nerve by using a protocol that maximally activates glucose transport. After treatment with insulin, contractions, or insulin plus contractions or no treatment, the gastrocnemius-plantaris-soleus muscle group was dissected out and was subjected to subcellular fractionation to separate the plasma membrane and intracellular membrane fractions. Insulin induced a 70% increase and contractions induced a 113% increase in the GLUT-4 content of the plasma membrane fraction. The effects of insulin and contractions were additive, as evidenced by a 185% increase in the GLUT-4 content of the sarcolemmal fraction. This finding provides evidence that the incremental effect of maximally effective insulin and contractile stimuli on glucose transport is mediated by additivity of their effects on GLUT-4 translocation into the sarcolemma.

Author (Hemer)

A95-74335

DECREASE IN VENTRICULAR STROKE VOLUME AT APNEA TERMINATION IS INDEPENDENT OF OXYGEN DESATURATION

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Patients with obstructive sleep apnea experience nocturnal

hemodynamic oscillations in association with repetitive respiratory events. Apnea termination (recovery) is accompanied by the nadir of arterial O_2 saturation ($\text{Sa}(\text{sub } \text{O}_2)$), changes in intrathoracic pressure, and arousal from sleep. To investigate separately the contributions of hypoxemia and of arousal from sleep to changes in cardiac function, we continuously measured left ventricular stroke volume (LVSV) and mean arterial pressure (MAP) in eight subjects with severe obstructive sleep apnea during two experimental conditions: (1) subjects slept without intervention for 1 - 2 h and then supplemental O_2 was administered to maintain $\text{Sa}(\text{sub } \text{O}_2)$ equal to or greater than 90% throughout the apnea-recovery cycle and (2) upper airway obstructions were abolished using nasal continuous positive airway pressure and subjects were aroused from sleep by an auditory signal. Recovery was associated with an increase in MAP and a decrease in LVSV both with and without supplemental O_2 . Arousal from sleep on nasal continuous positive airway pressure reproduced the postapneic elevation of MAP but not a decrease in cardiac function of the magnitude that occurred at apnea termination. We conclude that elevation of blood pressure and reduction of LOVSV that occurred at apnea termination may be due to different physiological mechanisms.

Author (Hemer)

A95-74336* National Aeronautics and Space Administration. Ames Research Center, Moffett Field, CA.

FORCE-VELOCITY AND POWER CHARACTERISTICS OF RAT SOLEUS MUSCLE FIBERS AFTER HINDLIMB SUSPENSION

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The effects of 1, 2, and 3 wk of hindlimb suspension (HS) on force-velocity and power characteristics of single rat soleus fibers were determined. After 1, 2, or 3 wk of HA, small fiber bundles were isolated, placed in skinning solution, and stored at -20 C until studied. Single fibers were isolated and placed between a motor arm and force transducer, functional properties were studied, and fiber protein content was subsequently analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). Additional fibers were isolated from soleus of control after 1 and 3 wk of HS, and fiber type distribution and myosin light chain stoichiometry were determined from SDS-PAGE analysis. After 1 wk of HS, percent type I fibers declined from 82 to 74%, whereas hybrid fibers increased from 10 to 18%. Percent fast type II fibers increased from 8% in control and 1 wk of HS to 26% by 3 wk of HS. Most fibers showed an increased unloaded maximal shortening velocity ($V(\text{sub } 0)$), but myosin heavy chain remained entirely slow type I. The mechanism for increased $V(\text{sub } 0)$ is unknown. There was a progressive decrease in fiber diameter and peak force after 1, 2, and 3 wk of HS, respectively. One week of HS resulted in a shift of the force-velocity curve, and between 2 and 3 wk of HS the curve shifted further such that $V(\text{sub } 0)$ was higher than control at all relative loads less than 45% peak isometric force. Peak absolute power output of soleus fibers progressively decreased through 2 wk of HS but showed no further change at 3 wk. The results suggest that between 2 and 3 wk the HS-induced alterations in the force-velocity relationship act to maintain the power output of single soleus fibers despite a continued reduction in fiber force.

Author (Hemer)

A95-74337

EFFICIENCY FUNCTION: IMPROVEMENT OF CLASSICAL BIOHEAT APPROACH

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In view of the complex vascular architecture and the intricate physical heat transfer processes in the human body, convective heat transfer via the blood is generally described by simple substi-

tutional processes ('nonvascular models'). The classical 'bioheat' approach of Pennes, (1948), defining the heat flow to or from the tissue as being proportional to the product of perfusion rate and the difference of arterial and tissue temperature, has been seriously questioned after having been used for greater than 40 yr in many applications. In our laboratory, we have at our disposal a complex three-dimensional vascular model for the special case of tissue in a human extremity. This was used to test the performance of simple nonvascular models. It turned out that the Pennes approach may deliver acceptable results if the body is in the thermoneutral zone or if heat stress acts uniformly on the whole body. However, when cold stress or local hyperthermia is present, unreliable results must be expected. As the vascular model is not generally practicable because of its extreme complexity, we offer the efficiency function concept as a simple way of correcting the classical bioheat approach by factor multiplication. Efficiency function is determined as a function of perfusion rate and tissue depth in a way that compensates for the deficiencies of the Pennes bioheat term. The results are reasonable compared with those of the vascular model and experimental results.

Author (Hemer)

A95-74338

EFFECT OF ELASTASE ON OSCILLATION MECHANICS OF LUNG PARENCHYMAL STRIPS

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Using isolated parenchymal strips from degassed rat lungs, we studied the contribution of the collagen-elastin network to lung tissue hysteretic behavior. Strips were suspended in an organ bath filled with Krebs solution continuously bubbled with 95% O₂ - 5% CO₂. One end of the strip was attached to a force transducer and the other to a servo-controlled lever arm. Sinusoidal oscillations of 2.5% of resting length were applied at 1 Hz. Measurements were sampled under baseline conditions at different levels of stress (σ = 10 - 26 g/cm). Porcine pancreatic elastase was then added to the bath, and tension and length were measured continuously for 15 min at σ = 15 g/cm. After washout, measurements were repeated at σ = 10 - 26 g/cm. Elastance (E) and resistance (R) were calculated using the equation of motion. Hysteresivity η , the structural damping coefficient, was obtained using the following equation: $\eta = (R/E \pi 2f)$, where f is frequency. At baseline, we found that E and R were significantly dependent on σ , whereas η was unchanged. During enzymatic digestion with elastase, there were significant decreases of tension, E, R and no change in η . Significant increases in E and R were found when these parameters were compared at the same σ before and after treatment. Again, η did not change. The constancy of η after elastase suggests that disruption of the elastin-collagen network does not alter the coupling between elastic and dissipative processes in lung tissue.

Author (Hemer)

A95-74339

STABILITY OF ALVEOLAR CAPILLARY OPENING PRESSURES

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Little is known about the stability of the process by which pulmonary capillaries open. To investigate this process, pulmonary

capillary perfusion patterns in isolated pump-perfused canine lobes were studied using video microscopy. After pump flow was set to perfuse one-half of the capillaries, the pump was turned off and all of the capillaries emptied. Turning the pump back on reopened the capillaries. The on-off cycle was repeated six times. If the same capillaries were perfused during each observation, it would demonstrate that there were stable and significant differences between individual capillary opening pressures, causing consistent recruitment of those capillaries with the lowest opening pressures. Alternatively, variable perfusion patterns would result if capillary opening pressures changed between observations, if the differences in opening pressures between capillary segments were negligible, or if experimental conditions changed between cycles. The perfusion pattern was more reproducible than expected by chance alone, which indicated the existence of stable differences among alveolar capillary opening pressures.

Author (Hemer)

A95-74340

EFFECT OF REGIONAL CIRCULATION PATTERNS ON OBSERVED HbCO LEVELS

MARJOLEIN V. SMITH, MILAN J. HAZUCHA, VERNON A. BENIGNUS, and PHILIP A. BROMBERG. *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1659-1665

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In an earlier experiment, we briefly exposed 15 young men to high levels of CO while simultaneously monitoring arterial and peripheral venous HbCO levels. The arterial HbCO levels were considerably higher than the venous levels during the CO exposure. Furthermore, great variation in the difference between arterial and venous HbCO levels was observed, with the maximal difference for each subject ranging from 2.3 to 12.1% HbCO. In the present paper, we suggest an explanation for the observed differences between arterial and venous HbCO on the basis of the regional circulation of the forearm, where both samples were taken. Because regional circulation patterns are known to vary with physical training, the differences in physical training between subjects may account for the observed variation. An expanded model was derived from the Coburn-Forster-Kane equation, which reflects the above hypothesis. Most of the parameter values for the expanded model were measured on individual subjects. Literature values were used for other parameters. Two parameters were estimated using five of the subjects and were then used in the predictions of the expanded model for the remaining subjects.

Author (Hemer)

A95-74341

REPRODUCIBILITY OF CORE TEMPERATURE THRESHOLD FOR SWEATING ONSET IN HUMANS

GEORGE L. BRENGELMANN, MARGARET V. SAVAGE, and DAVID H. AVERY. *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1671-1677

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The control of sweating in humans has been described quantitatively in terms of skin and core temperatures ($T_{\text{sub sk}}$ and $T_{\text{sub core}}$), respectively. However, the precision with which features of the relationship between sweat rate and $T_{\text{sub core}}$ at a given $T_{\text{sub sk}}$ can be reproduced in the short term is not known. We focused on the threshold $T_{\text{sub core}}$. We held $T_{\text{sub sk}}$ at 38°C until sweating began for two periods separated by a period of cooling with $T_{\text{sub sk}}$ at 32°C in six men and three women. The esophageal temperature ($T_{\text{sub es}}$) at which sweating began was invariably lower in the second period of heating. Also, the rate of rise in $T_{\text{sub es}}$ was invariably higher during the second period of heating. Thus, although a threshold cannot be reproduced within the error of $T_{\text{sub es}}$ measurement, the consistency and small magnitude of the downward shift recommend our protocol as a practical method for evaluating other influences on thermoregulation, provided that the effects are big enough to be seen against a background of an expected small decrease. From the fundamental point of view, the

consistency of the downward displacement has provocative implications, e.g., the rate of change in T(sub core) influences sweating or thermosensitive units in slow-responding thermal compartments contribute to the T(sub core) input signal. Author (Hemer)

A95-74342

EFFECTS OF STRENGTH TRAINING ON BONE MINERAL DENSITY: HORMONAL AND BONE TURNOVER RELATIONSHIPS

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The effects of a 16-wk strength-training program on bone mineral density (BMD) was assessed by dual-energy X-ray absorptiometry in 21 men. Sixteen men served as control subjects. To investigate the possible hormonal relationships underlying the effects on BMD, serum concentrations of growth hormone, insulin-like growth factor I, and testosterone were determined before and after training. In addition, osteocalcin and skeletal alkaline phosphatase (markers of bone formation) and tartrate-resistant acid phosphatase (a marker of bone resorption) were measured before and after training to assess bone turnover. The training program resulted in a $2.8 \pm 0.6\%$ increase in femoral neck BMD. However, there were no significant changes in total body, anteroposterior spine, lateral spine, Ward's triangle, or greater trochanter BMD. Moreover, there were no significant changes in growth hormone, insulin-like growth factor I, testosterone, osteocalcin, or skeletal alkaline phosphatase. There were no changes in the control group. Thus, strength training can increase femoral neck BMD, and this effect does not appear to be accompanied by changes in anabolic hormones or markers of bone formation and resorption.

Author (Hemer)

A95-74343

EFFECTS OF GLUCOCORTICOID AND ENDURANCE TRAINING ON CYTOCHROME OXIDASE EXPRESSION IN SKELETAL MUSCLE

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This investigation was undertaken to evaluate whether the mitochondrial dysfunction associated with glucocorticoid treatment is expressed at the level of cytochrome-c oxidase (COX) and whether endurance training attenuates this response. Adult female rats were administered cortisol acetate (100 mg/kg body wt) or an equal volume of the vehicle solution for 11 days. Endurance training was performed by treadmill running up to 28 m/min (with intervals at 50 m/min for 2 min every 15 min), for 90 min/day, 6 days/wk, for 8 - 10 wk. During hormone treatments, the training animals ran every day. Exercise prevented 43 - 55% of the hormone-induced atrophy in various fast-twitch muscles or muscle groups. Cortisol acetate treatment produced no significant effects on COX enzyme activities or submit mRNA content in deep red or superficial white quadriceps or mixed plantaris muscles. The levels of COX were increased as a result of training by 70 - 110% in plantaris and red quadriceps muscles, but no changes were seen in white quadriceps muscles. Both nuclear-encoded (COX IV) and mitochondrial-encoded (COX III) mRNAs were increased approximately twofold by the exercise program in these same muscles. These data indicate that the impaired mitochondrial functioning associated with glucocorticoids is not observed at the COX step of electron transport. The prolonged endurance-training regimen appears to induce relatively parallel increases in COX enzyme activity and mRNA expression with coordinate changes in nuclear and mitochondrial mRNAs.

Author (Hemer)

A95-74344

MAXIMAL AEROBIC CAPACITY AND TOTAL BLOOD VOLUME IN HIGHLY TRAINED MIDDLE-AGED AND OLDER FEMALE ENDURANCE ATHLETES

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The primary aim of this study was to test the hypothesis that, relative to age-matched sedentary controls, middle-aged and older female endurance athletes exhibit levels of maximal rate of O₂ consumption (dot-V(sub O₂ max)) similar to those previously reported in male endurance athletes in the same age group and, furthermore, that these high levels of dot-V(sub O₂ max) are associated with elevated total blood volumes. To accomplish this, we measured dot-V(sub O₂ max) and total blood volume in 13 highly trained female runners and 17 healthy untrained women 50 - 70 yr of age. The runners had lower body mass index and estimated body fat relative to the controls. They also had higher levels of dot-V(sub O₂ max) and total blood volume. The elevated total blood volumes in the runners were due to both higher plasma and erythrocyte volumes. In addition, hematocrit and hemoglobin concentrations were higher in the runners. Dot-V(sub O₂ max) was strongly related to total blood volume, plasma volume, and erythrocyte volume when all were expressed relative to body weight. These findings support the hypothesis that highly trained 50- to 70-yr-old female endurance athletes are capable of exhibiting levels of dot-V(sub O₂ max) approximately 85% higher on average than age-matched healthy untrained controls, consistent with previous findings in trained and untrained men of this age. Furthermore, the high levels of dot-V(sub O₂ max) in the athletes are associated with elevated total blood volumes.

Author (Hemer)

A95-74345

NMDA RECEPTORS IN CAUDAL VENTROLATERAL MEDULLA MEDIATE REFLEX AIRWAY DILATION ARISING FROM THE HINDLIMB

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The caudal ventrolateral medulla (CVLM) has been shown to participate in the reflex airway dilation evoked by stimulation of thin fiber afferents innervating the hindlimb of anesthetized dogs. Nevertheless, the pharmacological mechanism in the CVLM by which hindlimb afferents evoke this reflex airway dilation is not known. Therefore, we examined the role played by excitatory amino acid receptors in the CVLM in the reflex airway dilation arising from the hindlimb. Using chloralose-anesthetized dogs, we found that bilateral microinjections into the CVLM of either (+/-)-3-(2-carboxypiperazin-4-yl)-propyl-1-phosphonic acid or (+/-)-2-amino-5-phosphonopentanoic acid, both of which block N-methyl-D-aspartate (NMDA) receptors, reversibly attenuated the decrease in total lung resistance that was evoked by either electrical stimulation of C-fibers in the sciatic nerve or by static contraction of both gastrocnemius muscles. In contrast, bilateral microinjection into the CVLM of 6-cyano-7-nitroquinoxaline-2,3-dione, which blocks non-NMDA receptors, augmented the reflex decrease in total lung resistance that was evoked by either sciatic nerve stimulation or contraction of the gastrocnemius muscles. Bilateral microinjections of xanthurenic acid into the CVLM had no effect on the decrease in total lung resistance that was evoked by sciatic nerve stimulation. We conclude that NMDA, but not non-NMDA, receptors in the CVLM play an important role in the reflex arc that dilates the airways when

hindlimb afferents are stimulated by either muscular contraction or electrical stimulation. Author (Hemer)

A95-74346

ANALYSIS OF FACTORS AFFECTING GAS EXCHANGE IN INTRAVASCULAR BLOOD GAS EXCHANGER

S. C. NIRANJAN, JOHN W. CLARK, KA-YIU SAN, JOSEPH B. ZWISCHENBERGER, and AKHIL BIDANI Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1716-1730 Research sponsored by Texas Univ. Medical Branch, Moody Foundation, and Shriners Hospital for Crippled Children (HTN-95-A0645) Copyright

A mathematical model of an intravascular hollow-fiber gas-exchange device, called IVOX, has been developed using a Krogh cylinder-like approach with a repeating unit structure comprised of a single fiber with gas flowing through its lumen surrounded by a coaxial cylinder of blood flowing in the opposite direction. Species mass balances on O₂ and CO₂ result in a nonlinear coupled set of convective-diffusion parabolic partial differential equations that are solved numerically using an alternating-direction implicit finite-difference method. Computed results indicated the presence of a large resistance to gas transport on the external (blood) side of the hollow-fiber exchanger. Increasing gas flow through the device favored CO₂ removal from but not O₂ addition to blood. Increasing blood flow over the device favored both CO₂ removal as well as O₂ addition. The rate of CO₂ removal increased linearly with the transmural PCO₂ gradient imposed across the device. The effect of fiber crimping on blood phase mass transfer resistance was evaluated indirectly by varying species blood diffusivity. Computed results indicated that CO₂ excretion by IVOX can be significantly enhanced with improved bulk mixing of vena caval blood around the IVOX fibers. Author (Hemer)

A95-74347

PMN CELL COUNTS AND PHAGOCYTIC ACTIVITY OF HIGHLY TRAINED ATHLETES DEPEND ON TRAINING PERIOD

V. HACK, G. STROBEL, M. WEISS, and H. WEICKER Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1731-1735

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We tested the hypothesis that polymorphonuclear leukocyte (PMN) cell counts and phagocytic activity determined by latex ingestion and superoxide anion production are influenced by different training periods. We investigated long-distance runners before and up to 24 h after a graded exercise test to exhaustion during moderate training (MT) and intense training (IT) and compared them with untrained (control) subjects. Cell counts and phagocytic activity at rest and after exercise did not differ significantly between MT and control. On the contrary, IT showed a significant decrease in PMN cell count at rest compared with MT and control. Furthermore, phagocytic activity was significantly reduced in IT at rest and after exercise compared with MT and control. A strong inverse correlation between epinephrine and superoxide anion production was found. These results provide evidence that the phagocytic activity depends on the training period and indicate impaired PMN functions during IT, which might lead to increased susceptibility to infection.

Author (Hemer)

A95-74348

VOLUNTARY EXERCISE DECREASES PROGRESSION OF MUSCULAR DYSTROPHY IN DIAPHRAGM OF MDX MICE

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Effects of voluntary wheel running on contractile properties of diaphragm (DIA) and soleus (SOL) of dystrophic (mdx) and control (C57BL/10SNJ) mice were evaluated. In particular, we tested the hypothesis that daily voluntary running is not deleterious to muscle

function in mdx mice. Both groups of mice ran extensively. Exercise increased maximal specific tetanus tension of mdx DIA from 1.02 \pm 0.04 to 1.33 \pm 0.06 kg/sq cm but did not restore it to the control level. Maximal tetanus tension of sedentary mdx SOL was reduced compared with control and was not altered by running activity. Optimal length was significantly lower in DIA of mdx mice, and exercise did not change this. Fatigability and contractile properties of muscles measured in vitro were not altered by running activity with the exception of increased contraction time in mdx DIA. In conclusion, extensive wheel running is not deleterious to muscle function in mdx mice contrary to predictions of the 'work overload' theory of muscular dystrophy. Rather, this exercise is beneficial for active tension generation of mdx DIA, the muscle most closely resembling muscles of patients with Duchenne muscular dystrophy.

Author (Hemer)

A95-74349

MUSCLE ENERGETICS AND PULMONARY OXYGEN UPTAKE KINETICS DURING MODERATE EXERCISE

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The present study tested whether, during moderate exercise, (1) the dynamic responses of ADP and changes in free energy of ATP hydrolysis ($\Delta G(\text{sub ATP})$) were similar to those of phosphocreatine and (2) the rise in pulmonary O₂ uptake ($\dot{V}(\text{sub O}_2)$) during cycle exercise would reflect the rise in muscle $\dot{Q}(\text{sub O}_2)$ indicated by the calf PCr kinetics. The responses of PCr, P(_{sub i}), ADP, and $\Delta G(\text{sub ATP})$ were measured from the calf in five subjects during supine treadmill exercise using P-31-magnetic resonance spectroscopy and compared with those for $\dot{V}(\text{sub O}_2)$, measured breath by breath during upright cycle exercise. The time constants for $\Delta G(\text{sub ATP})$ were not significantly different from those for PCr and P(_{sub i}). The time constants for phase 2 $\dot{V}(\text{sub O}_2)$ were also similar to those of PCr. In contrast, the dynamics of ADP were distorted from those of PCr due to dynamic changes in pH. These results are consistent with mechanisms of respiratory control that feature substrate control by PCr or thermodynamic control through changes in $\Delta G(\text{sub ATP})$. However, these results are not consistent with substrate control by ADP in a simple fashion. Furthermore, the similarity of time constants for phase 2 $\dot{V}(\text{sub O}_2)$ and muscle PCr suggests that phase 2 $\dot{V}(\text{sub O}_2)$ kinetics reflect those of muscle $\dot{Q}(\text{sub O}_2)$ in healthy subjects during moderate exercise.

Author (Hemer)

A95-74350

SODIUM TRANSPORT AND FLUID BALANCE IN LUNGS FROM NORMAL AND DYSTROPHIC HAMSTERS

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Gravimetric and sodium transport characteristics of lungs from BIO 14.6 (dystrophic) hamsters were compared with those of lungs from golden Syrian (normal) hamsters at 30 and 150 days of age. Isolated perfused lungs were used to determine lung permeability and fluid balance differences between normal and dystrophic animals at both ages. Apparent permeability-surface area products for air space-to-vascular space sodium, sucrose, and fluorescein isothiocyanate-labeled dextran fluxes were compared in the four groups of hamsters. Morphometric analysis of fixed lungs of representative hamsters from

each group was also performed. Dystrophic hamsters exhibited higher lung wet-to-dry weight ratios than normal hamsters at both ages. Lungs from dystrophic hamsters were less sensitive to inhibition of sodium transport by amiloride than lungs from age-matched normal hamsters. Dystrophic hamster lungs had higher absolute permeabilities of the passively transported solutes, lower permeability values for sodium, and only one-half of the amiloride-sensitive sodium transport of lungs from age-matched normal hamsters. Differences in lung fluid balance between dystrophic and normal hamsters may be related to differences in sodium clearance.

Author (Hemer)

A95-74351

EFFECTS OF LUNG VOLUME AND SURFACE FORCES ON MAXIMAL AIRWAY SMOOTH MUSCLE SHORTENING

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The effects of lung volume and surface forces on airway smooth muscle shortening were studied in isolated perfused rat lungs. The lungs were inflated via the trachea with gas or Krebs solution to volumes equivalent to gas inflation pressures of 5 (low), 15 (medium), and 25 (high) cmH₂O. At each volume, two of the four lungs were perfused with methacholine and then all were perfused with Formalin for fixation. The amount of smooth muscle shortening present in transverse sections of the airways was determined by comparing the observed outer perimeter of the smooth muscle layer with its calculated relaxed perimeter. In the control lungs, mean shortening was less than or equal to 10% in all groups except the liquid-filled lungs at low lung volumes. In the methacholine-stimulated lungs, mean shortening was between 45 and 56% at medium and low lung volumes in gas- and liquid-filled lungs, respectively, and approximated the degree of shortening required to cause airway closure. At high lung volume, less shortening was observed in the methacholine-stimulated lungs, either liquid or gas filled. The effects of lung volume in liquid-filled lungs and the differences in response between gas- and liquid-filled lungs demonstrate, respectively, that both lung tissue recoil and surface forces act to oppose shortening of maximally stimulated smooth muscle. However, the finding that airway closure is not prevented at medium and low lung volumes suggests that additional factors are also important in limiting airway smooth muscle shortening in vivo.

Author (Hemer)

A95-74352

EFFECT OF AMINOPHYLLINE ON PLASMA (K(+)) AND HYPOXIC VENTILATORY RESPONSE DURING MILD EXERCISE IN MEN

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To examine the role of endogenous adenosine on the hypoxic ventilatory response (HVR) enhanced during exercise, we measured HVR at rest and during mild exercise (12.5 W) in nine healthy men in a supine position after pretreatment with aminophylline (5 mg/kg), an adenosine receptor blocker, or dipyrindamole (0.6 mg/kg), an adenosine uptake blocker, by using a 3-day double-blind placebo-controlled design. Although HVR was enhanced during exercise on all occasions, HVR with aminophylline was significantly lower than that with placebo or dipyrindamole during exercise at similar end-tidal P(sub CO₂) on the 3 days but not at rest. We then examined the changes in plasma K(+) concentration (K(+)) and

catecholamines, the other possible endogenous potentiators of the carotid body activity. The exercise- and hypoxia-induced increases in plasma (K(+)) were significantly lower with aminophylline than with the placebo or dipyrindamole. We therefore conclude that aminophylline attenuates the enhancement of HVR during mild exercise and that this might be due to its attenuating effect on exercise- and hypoxia-associated increases in plasma (K(+)) rather than due to its antagonizing effect on endogenous adenosine.

Author (Hemer)

A95-74353

MECHANICS OF HUMAN QUADRICEPS MUSCLE

CATHERINE COIRAUT, BRUNO RIOU, NATHALIE PERY-MAN, ISABELLE SUARD, and YVES LECAROENTIER *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1769-1775 Research sponsored by Fondation pour la Recherche Medicale and Association Francaise contre les Myopathies (HTN-95-A0652) Copyright

Mechanics of human quadriceps muscle strips (vastus lateralis; n = 10) were investigated over the whole load continuum. Mechanical experiments were performed at 29 C and in both twitch and tetanus modes. For a given level of isotonic total load (P) and over a large part of the contraction phase, instantaneous velocity (V) was shown to be a unique function of instantaneous length (L), regardless of time and initial length. By considering this time- and initial length-independent mechanical property between instantaneous L and instantaneous V over the whole P continuum, a three-dimensional P-V-L relationship was constructed. Any variations in stimulation conditions modified the time-independent P-V-L diagram. Such modifications in the P-V-L relationship were characteristic of changes in contractile performance. Moreover, characteristics of the P-V relationship were investigated in both twitch and tetanus modes. The curvature of the P-V hyperbola was significantly higher in tetanus at 30 Hz than in twitch mode. In conclusion, our study indicates that, in human quadriceps muscles, contractility can be defined as the time- and initial length-invariant part of a three-dimensional P-V-L relationship. Moreover, our data are consistent with an increase in economy of force generation in tetanus contractions compared with that in twitches.

Author (Hemer)

A95-74355

BIOENERGETIC APPROACH TO TRANSFER FUNCTION OF HUMAN SKELETAL MUSCLE

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A mathematical model analogous to Chance's 'transfer function' was derived on the basis of the energy consumption principle, which is suitable to describe the energetics of human skeletal muscle during aerobic activity. The implications and characteristics of this model are that (1) the half time of phosphocreatine (PCr) hydrolysis at the onset of a mechanical constant-load exercise is independent of the imposed charge, (2) the changes of O₂ consumption in the muscle at steady state when changing workload are linearly related to PCr concentration, (3) the kinetics of the intracellular oxygen consumption during a rest-to-work transient are influenced by anaerobic glycolysis, (4) it may explain the PCr-time relationship of different muscles types (e.g., skeletal, heart, trained vs. untrained), (5) it allows one to interpret correctly the significance of the oxygen consumption kinetics in the rest-to-work transient at the lung level, and (6) it is conceived for in vivo applications.

Author (Hemer)

A95-74356

CAPACITY FOR RED BLOOD CELL AGGREGATION IS HIGHER IN ATHLETIC MAMMALIAN SPECIES THAN IN SEDENTARY SPECIES

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KAMENEVA Pittsburgh Univ., Pittsburgh, PA, US, and MARGARET A. WILD Wildlife Research Center, Fort Collins, CO, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1790-1794

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The purpose of this study was to show that two rheological parameters, red blood cell (RBC) sedimentation rate and apparent blood viscosity at low shear rate, characterizing the degree of RBC aggregation, correlate significantly with the maximal mass-specific rate of oxygen consumption or aerobic capacity (dot-VO(sub 2 max)). Comparisons were made within two groups of similarly sized athletic and sedentary species: group 1, pronghorn antelope, dog, goat, and sheep; and group 2, horse and cow. The pronghorn antelope (*Antilocapra americana*) is one of the most athletic mammals, and we have obtained data on the rheological properties of blood from this species for the first time. The values of apparent viscosity at hematocrit = 40% and shear rate = 0.277/s measured in a rotational viscometer were 59.5, 42.6, and 9.1 cP for antelope, dog, and sheep blood respectively, and 55.3 and 11.5 cP for horse and cow blood, respectively. The viscosity values for antelope, dog, and sheep blood can be correlated with aerobic capacity: $\ln \text{viscosity} = 4.48 - 106.3/\text{dot-V sub}(O_2 \text{ max})$. The values of RBC sedimentation rate at hematocrit = 40% were 12.8, 7.0, and 0 mm/h for antelope, dog, and sheep blood respectively, and 45.3 and 0.1 mm/h for horse and cow blood, respectively. Therefore, the data showed that the athletic species exhibit a consistently higher degree of RBC aggregation than do the corresponding nonathletic species.

Author (Hemer)

A95-74357

ERYTHROCYTE AND POLYMORPHONUCLEAR CELL TRANSIT TIME AND CONCENTRATION IN HUMAN PULMONARY CAPILLARIES

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Pulmonary capillary transit times were examined in patients who required lung resection by use of Tc-99m-labeled macroaggregates (Tc-99-MAA) and chromium-labeled erythrocytes (Cr-51-RBC) to measure regional blood flow and volume in the resected lung. Cell flow to each resected lung sample was determined by multiplying the number of polymorphonuclear leukocytes (PMN) per milliliter of circulating blood by the blood flow to that sample. Capillary blood volume was obtained by multiplying the morphometrically determined fraction of pulmonary blood in capillaries by the total Cr-51-RBC volume in each sample. Cell concentrations (cells/ml) in capillary blood were calculated morphometrically, and capillary transit times were obtained by dividing cell concentration by cell flow. The results show that PMN transit times were 60 - 100 times longer than the RBC transit times, with a 22% overlap between their distributions. We conclude that PMN are concentrated with respect to RBC in pulmonary capillary blood because of differences in their transit times and that these long transit times provide an opportunity for PMN-endothelial interactions. Author (Hemer)

A95-74358

RHEOLOGICAL RESPONSE OF NEUTROPHILS TO DIFFERENT TYPES OF STIMULATION

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LOCKWOOD, R. HATTON, and G. B. NASH Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1801-1810 Research sponsored by Medical Research Council and Zeneca Pharmaceuticals

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The potential for neutrophils to obstruct microvessels was evaluated by measuring transit of individual neutrophils through 8-micrometer pores in an automated cell transit analyzer (CTA) or into micropipettes (4 - 8 micrometer ID). Stimulation *in vitro* by the chemotactic agent N-formyl-methionyl-leucyl-phenylalanine (fMLP), cigarette smoke, or purified antineutrophil cytoplasm antibodies greatly increased flow resistance, but the response varied in its dependence on time and pore diameter. Cigarette smoke or fMLP caused rapid loss of cellular deformability, although observations were complicated by changes in cell shape: progressive bipolar shape formation (after treatment with fMLP) could facilitate entry into larger pores (approximately 8 micrometer), whereas blebs induced by cigarette smoke caused bridging of these pores with cell immobilization. These processes led to an underestimation of the changes in deformability by the CTA. Neutrophils responded slowly to the antineutrophil cytoplasm antibodies (approximately 30 min), with a greater increase in flow resistance evaluated by a micropipette (4 - 6 micrometer ID) than by the CTA. We conclude that the effect of neutrophil stimulation on flow through capillary-sized vessels is potentially great (with resistance typically increased 10-fold or even complete blockage) but may depend on the vascular and cellular geometry and may be local or disseminated, depending on the rate of the rheological response. Author (Hemer)

A95-74359

MODIFICATION OF FOREARM RESISTANCE VESSELS BY EXERCISE TRAINING IN YOUNG MEN

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The aim of this study was to determine whether a 4-wk handgrip training program would elicit changes in endothelium-dependent and endothelium-independent vasodilatation in resistance vessels of the human forearm. Minimum vascular resistance after a 10-min ischemic stimulus, an index of peak vasodilator capacity, was also determined. Forearm blood flow response to the endothelium-dependent vasodilator methacholine chloride did not change over the 4-wk intervention period either in the group undertaking training (n = 11) or in control subjects (n = 6). Similarly, the response to sodium nitroprusside was not influenced by the handgrip training program. Peak vasodilator capacity of the trained forearms significantly increased, whereas no change was evident in the untrained limbs. These results suggest that 4 wk of forearm exercise training enhances peak vasodilator capacity of the vasculature without influencing stimulated activity of the nitric oxide dilator system. Author (Hemer)

A95-74360

EFFECT OF PULMONARY BLOOD FLOW ON MICROVASCULAR PRESSURE PROFILE DETERMINED BY MICROPUNCTURE IN PERFUSED CAT LUNGS

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To clarify the role of the pulmonary microvasculature in adjusting to increased pulmonary blood flow, we measured arteriolar and venular pressure by the servo-null micropuncture method while changing the pulmonary blood flow in isolated perfused cat lungs.

We divided the lung vasculature into three longitudinal segments: (1) arterial, (2) microvascular, (3) venous. The vascular resistance was calculated by dividing the pressure gradient by the flow. The pressure gradient of the microvascular segment did not increase, whereas the pressure gradient of the arterial and venous segments increased simultaneously with flow rate. Total and microvascular resistance decreased with increase of flow rate. Resistances of the arterial and venous segments did not change with increase in flow. We conclude that the microvasculature plays a crucial role in preventing pulmonary hypertension with increases in flow by decreasing microvascular resistance.

Author (Hemer)

A95-74361

LACTATE TRANSPORT STUDIED IN SARCOLEMMA GIANT VESICLES FROM HUMAN MUSCLE BIOPSIES: RELATION TO TRAINING STATUS

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The present study examined sarcolemmal lactate transport capacity in humans of widely different training status. Muscle biopsies were obtained from m. vastus lateralis in 39 subjects divided into untrained, trained, and athlete (sprint runners, endurance runners, triathletes, and road and track bicyclists) groups. From the biopsy sample giant vesicles were produced with collagenase treatment to determine the sarcolemmal lactate transport capacity, and histochemical analyses were made. The athletes had a higher capacity to transport lactate than the untrained and trained subjects. Within the group of athletes, the bicyclists had a higher lactate transport capacity than the runners, whereas there was no difference among trained subjects, runners, and triathletes. The lactate transport capacity was related to the occurrence of type I muscle fibers. The present results suggest that the capacity to transport lactate is higher in athletes than in untrained and less trained subjects. It might indicate that lactate transport capacity in human skeletal muscle can be changed by a high volume of training including frequent high-intensity sessions. In addition, sarcolemmal lactate transport capacity appears to be related to the fiber type distribution of a muscle.

Author (Hemer)

A95-74362* National Aeronautics and Space Administration. John F. Kennedy Space Center, Cocoa Beach, FL.

ALTERED THERMOREGULATORY RESPONSES AFTER 15 DAYS OF HEAD-DOWN TILT

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To determine whether extended exposure to a simulation of microgravity alters thermoregulatory reflex control of skin blood flow, six adult males were exposed to 15 days of 6 deg head-down tilt (HDT). On an ambulatory control day before HDT exposure and on HDT day 15 the core temperature of each subject was increased by 0.5 - 1.0 °C by whole body heating with a water-perfused suit. Mean skin temperature, oral temperature (T_{sub or}), mean arterial pressure, and forearm blood flow were measured throughout the protocol. Forearm vascular conductance (FVC) was calculated from the ratio of forearm blood flow to

mean arterial pressure. After HDT exposure, the T_{sub or} threshold at which reflex thermally induced increases in FVC began was elevated, whereas the slope of the T_{sub or}-FVC relationship after this threshold was reduced. Moreover, normothermic FVC and FVC at the highest common T_{sub or} between pre- and post-HDT trials were reduced after HDT. These data suggest that HDT exposure reduces thermoregulatory responses to heat stress. The mechanisms resulting in such an impaired thermoregulatory response are unknown but are likely related to the relative dehydration that accompanies this exposure.

Author (Hemer)

A95-74363

ANATOMY OF MEMBRANOUS BRONCHIOLES IN NORMAL, SENILE, AND EMPHYSEMATOUS HUMAN LUNGS

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Serial reconstructions of the membranous bronchioles (MB) were performed in randomly selected tissue blocks cut parallel to the pleural surface in fixated human lungs. Two to four normal, senile, and emphysematous lungs were examined. Three (2 in senile lungs) orders of MB were observed with a dichotomous branching pattern. Emphysematous lungs are characterized by an overall decrease in airway diameter with localized stenoses. Comparison with mean airway diameter (bar-d) and density (bar-n (no. of MBs per sq cm of lung tissue)) of MBs obtained using standard morphometric techniques showed that the values of bar-d and bar-n are biased because of the inclusion in the measurements of a number of respiratory bronchioles and bronchi. When these misclassifications are corrected for, it appears that bar-d corresponds quite well to the mean diameter of the terminal bronchioles (TB) and bar-n to approximately twice the density of TBs. After correction, bar-n is not significantly reduced in emphysematous lungs (the grossly destroyed areas being excluded) compared with normal lungs. The estimate of the number of TBs obtained from the present data is markedly less than calculated by Weibel (1963), which suggests that the number of bronchi was overestimated by Weibel by at least one generation. Finally, values of peripheral airway resistance computed from the present anatomic data correspond quite well to direct measurements performed on the same lungs before fixation.

Author (Hemer)

A95-74364

HUMAN SKELETAL MUSCLE ADAPTATION IN RESPONSE TO CHRONIC LOW-FREQUENCY ELECTRICAL STIMULATION

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The purpose of the study was to verify the influence of several weeks of chronic low-frequency electrical stimulation (LFES) on the metabolic profile and functional capacity of human skeletal muscle. Knee extensor muscles (KEM) of eight subjects were electrically stimulated at 8 Hz for 8 h/day and 6 days/wk. Vastus lateralis muscle samples were taken before, after 4 wk, and after 8 wk of LFES, and activities of anaerobic (creatine kinase, phosphofructokinase, glyceraldehyde-3-phosphate dehydrogenase) and aerobic-oxidative (citrate synthesis, 3-hydroxyacyl-CoA dehydrogenase, cytochrome-c oxidase) enzyme markers were determined. KEM dynamic performance was also assessed before, after 4 wk, and after 8 wk of LFES. Activity levels of anaerobic enzymes were not altered, whereas the activity levels of citrate synthase (29%), 3-hydroxyacyl-CoA dehydrogenase (22%), and cytochrome-c oxidase (25%) were signifi-

cantly increased after 4 wk of LFES but were not further increased after 4 additional wk of LFES. KEM performance was also improved but leveled off after 4 wk of LFES. Although significant changes were observed, the results of the present study suggest that the muscle characteristic investigated in the current study have a limited capacity of adaptation in response to this form of chronic LFES.

Author (Herner)

A95-74365

MUSCLE LACTATE METABOLISM IN RECOVERY FROM INTENSE EXHAUSTIVE EXERCISE: IMPACT OF LIGHT EXERCISE

J. BANGSBO, T. GRAHAM, L. JOHANSEN, and B. SALTIN *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1890-1895 Research sponsored by Team Denmark, Danish Natural Science Foundation, Danish National Research Foundation, Brandts Legat, and NSERC (HTN-95-A0664) Copyright

This study examined the effect of low-intensity exercise on lactate metabolism during the first 10 min of recovery from high-intensity exercise. Subjects exercised one leg to exhaustion, and after 1 h of rest they performed the same exhaustive exercise with the other leg. For one leg the intense exercise was followed by rest (passive (P) leg), and for the other leg the exercise was followed by a 10-min period with low-intensity exercise at a work rate of 10 W (active (A) leg). The muscle lactate concentration after the intense exercise was the same in the P and A legs, but after 10 min of recovery, the lactate concentration and the arterial blood lactate level were higher for the P leg than for the A leg. During the recovery, the mean blood flow was lower for the P leg than for the A leg, whereas the mean lactate efflux was not significantly different. During the 10 min of recovery, lactate release accounted for approximately 60% of the change in muscle lactate for either leg. The leg excess postexercise O₂ consumption during 10 min of recovery was 440 and 750 ml for the P and A legs, respectively. The present data suggest that a lowered blood lactate level during active recovery is due to an elevated muscle lactate metabolism and is not caused by a transient higher release of lactate from the exercising muscles coupled with greater uptake in other tissues. Furthermore, with either mode of recovery muscle lactate does not appear to be a major substrate for glycogen synthesis and muscle glycogenesis seems to be a minor contributor to excess postexercise O₂ consumption.

Author (Herner)

A95-74366

EFFECT OF ARTERIAL BLOOD PRESSURE AND VENTILATION GASES ON CARDIAC DEPRESSION INDUCED BY CORONARY AIR EMBOLISM

J. H. VAN BLANKENSTEIN, C. J. SLAGER, L. K. SOEI, H. BOERSMA, and P. D. VERDOUW *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1896-1902 Research sponsored by Netherlands Heart Foundation (HTN-95-A0665) Copyright

In this study the time course of cardiac depression after selective intracoronary injection of air bubbles was investigated in six anesthetized pigs (30 \pm 2 kg) with different mixtures of ventilation gases and different mean arterial blood pressures (MAP). Air bubbles of 150 micrometer diam were injected into the left anterior descending coronary artery (LADCA) in a volume of 2 microliter/kg body wt. In each animal an injection of air bubbles was applied during ventilation with N₂-O₂ and a MAP of 77 \pm mmHg (N₂-O₂/low pressure) or 111 \pm 3 mmHg (N₂-O₂/high pressure) and during ventilation with pure O₂ and a MAP of 77 \pm mmHg (O₂/low pressure) or 110 \pm 3 mmHg (O₂/high pressure). Systemic hemodynamic variables such as left ventricular pressure, its peak first derivative, and MAP changed less than 10% after injection of air bubbles. During N₂-O₂/low pressure, systolic segment length shortening in the LADCA region (SS-LADCA) decreased from baseline

and did not return to baseline within the 10 min after injection of air bubbles. During N₂-O₂/high pressure and O₂/low pressure, SS-LADCA was increased between 60 and 120 s, whereas for O₂/high pressure this period was from 60 to 90 s. By calculating the time integral of the deviation from baseline of SS-LADCA, it could be demonstrated that the depression of regional myocardial function was less severe during O₂/high pressure and O₂/low pressure than during N₂-O₂/low pressure. We conclude that, when coronary air embolism occurs during hypertension and during ventilation with pure O₂ instead of a normal N₂-O₂ mixture, the resulting depression of regional myocardial function is reduced.

Author (Herner)

A95-74367

PREDICTION OF CENTRAL NERVOUS SYSTEM OXYGEN TOXICITY IN RATS

R. ARIELI Israel Naval Medical Inst., Haifa, Israel and G. HERSHKO Israel Naval Medical Inst., Haifa, Israel *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1903-1906 (HTN-95-A0666) Copyright

Cumulative O₂ toxicity (K) can be calculated using the expression $K = t(\exp 2) \times P(\text{sub O}_2 \exp c)$, where t is exposure time and the power c is to be determined; the phenomenon is liable to occur when K reaches K_c, the threshold value of K at which a symptom is manifested. Six rats were each exposed six times to 6 ATA O₂ at 2-day intervals until the first electrical discharge (FED) was noted in an electroencephalogram. There was no difference in latency to FED in the series of six exposures. Thirteen rats were exposed to O₂ until FED was noted in an electroencephalogram. They were exposed to four constant P(sub O₂)'s of 5, 6, 7, and 8 ATA and to two combined profiles of (1) 5 min at 7 ATA followed by 5 ATA and (2) 15 min at 5 ATA followed by 7 ATA. The solution of the equation for each rat was used to predict its latency to FED on the combined profile. The correlation of predicted to measure latency was significant, and the slope was not different from 1. Solving for these parameters using the combination of all the data, we obtained $K_c = 5.71 \times 10(\exp 6)$ and $c = 5.39$, which correctly predicted the mean latency but failed to predict individual latency. It is preferable to use each rat as its own control. The significance of the correlation supports the validity of the power equation for calculating K.

Author (Herner)

A95-74368

VENTILATORY AND HYPERKALEMIC RESPONSES TO INCREMENTAL EXERCISE AFTER PROPRANOLOL TREATMENT

DONALD A. SCHNEIDER, MICHAEL T. MCENIERY, COLIN SOLOMON, JAAK JURIMAE, and MARCUS S. WEHR *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1907-1912 (HTN-95-A0667) Copyright

The purpose of the present study was to examine the relationship of plasma potassium (K(+)) and minute ventilation (dot-VE) during incremental cycling (20 W/2 min) under conditions of beta-adrenergic blockade (80 mg of propranolol) and placebo in six untrained male subjects. No significant differences existed between treatments in O₂ uptake, CO₂ production, blood lactate, pH, or dot-VE during the submaximal work stages of incremental exercise common to both treatments (20 - 220 W). During exercise with beta-blockade, plasma K(+) concentrations were found to be significantly elevated compared with control levels at every work stage except 20 W. Significant positive correlations between dot-VE and plasma K(+) were found during both beta-blockade and control conditions. Although the high correlation between dot-VE and K(+) was not altered with beta-blockade, propranolol treatment resulted in a significant reduction in the slope of this relationship during incremental exercise. These findings suggest that (1) beta-blockade decreases the dot-VE-K(+) relationship observed during exercise and (2) K(+) stimulation of muscle afferents is not an important signal in the control of exercise ventilation.

Author (Herner)

A95-74369

ACIDOSIS STIMULATES BETA-ENDORPHIN RELEASE DURING EXERCISE

DEREK V. TAYLOR, JAMES G. BOYAJIAN, NORMAN JAMES, DANETTE WOODS, ALEKSANDRA CHICZ-DEMET, ARCHIE F. WILSON, and CURT A. SANDMAN *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1913-1918 (Contract(s)/Grant(s): NIH-R01-HD-28413-01) (HTN-95-A0668) Copyright

Elevated blood levels of beta-endorphin have been associated with high-intensity exertion, but the stimulus for beta-endorphin release is unknown. Some studies of exercise have associated beta-endorphin release with increased exertion levels, but other evidence suggests that acidosis may stimulate the release of beta-endorphin. This study examines acidosis as a possible stimulus for beta-endorphin release by examining the effects of arterial blood gases, whole blood lactate, and respiratory changes on beta-endorphin levels and by examining the effects of buffering during exercise on these levels. Initially, seven healthy adult males were evaluated during incremental exercise. During incremental exertion, indicators of acidosis correlated with endorphin levels: pH, $P(\text{sub CO}_2)$, HCO_3^- ($r = -0.88$), base excess, and lactate. A multivariate model showed that beta-endorphin levels were predicted best by the change in base excess. A time course analysis showed that beta-endorphin responses peaked postexercise and paralleled blood acid levels. Subsequently, subjects were compared after alkali loading and placebo during constant-intensity exercise at 85% of maximal exertion to determine whether acidosis is necessary for endorphin release. Treatment with a buffer, which effectively maintained pH above 7.40, significantly suppressed endorphin release. The results of this study indicate that acidosis rather than any other physiological change associated with high-intensity exertion is the primary stimulus for beta-endorphin release. Author (Hemer)

A95-74370* National Aeronautics and Space Administration. Ames Research Center, Moffett Field, CA.

EFFECT OF WATER TEMPERATURE ON DIURESIS-NATRIURESIS: AVP, ANP, AND URODILATIN DURING IMMERSION IN MEN

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Effects of water temperature on diuresis, natriuresis, and associated endocrine responses during head-out immersion were studied in eight men during four 5-h experimental conditions: air control at 28 C and immersion at 34.5 C (thermoneutral (Tnt)), 36 C (above Tnt (aTnt)), and 32 C (below Tnt (bTnt)). Esophageal temperature decreased by approximately 0.4 C in bTnt and increased by approximately 0.5 C in aTnt. Cardiac output increased by approximately 80% in aTnt and approximately 40% in bTnt while thoracic impedance, an index of central blood pooling, decreased by 7.5 ohms in bTnt (NS vs. Tnt) and 8.8 ohms in aTnt. Total peripheral resistance decreased at all temperatures (50% in aTnt, 20% in bTnt). Urine flow and Na^+ excretion increased by sixfold in bTnt and Tnt but by only threefold in aTnt. Creatinine clearance was unchanged while osmolal clearance (but not free water clearance) increased two-fold with all immersions. Plasma atrial natriuretic peptide (ANP), urinary urodilatin, and urinary guanosine 3',5'-cyclic monophosphate increased while plasma renin activity, aldosterone, and arginine vasopressin (AVP) decreased similarly at all temperatures. bTnt did not potentiate diuresis by selective attenuation of AVP. The overall natriuretic response exhibited a higher correlation with urodilatin than with ANP. Because diuresis and natriuresis were significantly attenuated in aTnt where central blood pooling was

greater, we conclude that mechanisms other than the atrial stretch receptor reflex, i.e., urodilatin and effective arterial blood volume, may play more predominant roles in the mechanism of immersion-induced diuresis and natriuresis. Author (Hemer)

A95-74371

CONTRACTILE AND CELLULAR REMODELING IN RABBIT SKELETAL MUSCLE AFTER CYCLIC ECCENTRIC CONTRACTIONS

RICHARD L. LIEBER, MARY C. SCHMITZ, DEV K. MISHRA, and JAN FRIDEN *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1926-1934 Research sponsored by Veterans Affairs and Swedish Medical Research Council (Contract(s)/Grant(s): NIH-AR-40050) (HTN-95-A0670) Copyright

The time course of muscle contractile and cellular properties was studied in rabbit ankle flexor muscles after injury produced by eccentric exercise. Cyclic eccentric exercise was produced by increasing the tibiotarsal angle of the rabbit while activating the peroneal nerve by use of transcutaneous electrodes. Muscle properties were measured 1, 2, 3, 7, 14, and 28 days after exercise to define the time course of muscle changes after injury. A control group receiving only isometric contraction was used to study the effect of cyclic activation itself. The magnitude of the torque decline after 1 day was the same with use of isometric or eccentric exercise, but eccentric exercise resulted in a further decrease in torque after 2 days, at which time isometrically exercised muscles had fully recovered. The most prominent morphological changes in the injured muscle fibers were the loss of antibody staining for the desmin cytoskeletal protein and deposition of intracellular fibronectin, even when the injured muscle fibers retained their normal complement of contractile and enzymatic proteins. The presence of fibronectin inside the myofibers indicated a loss of cellular integrity. Invasion by inflammatory cells was apparent on the basis of localization of embryonic myosin. Thus eccentric exercise initiates a series of events that results in disruption of the cytoskeletal network and an inflammatory response that could be the mechanism for further deterioration of the contractile response. Author (Hemer)

A95-74372

OXYGEN UPTAKE KINETICS IN CARDIAC TRANSPLANT RECIPIENTS

DONALD H. PATERSON, DAVID A. CUNNINGHAM, J. GEOFFREY PICKERING, MARK A. BABCOCK, and DEREK R. BOUGHNER *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1935-1940 Research sponsored by NSERC and Heart and Stroke Foundation of Ontario (HTN-95-A0671) Copyright

Our purpose was to examine the gas exchange response to exercise in heart transplant (HT) patients and to characterize the O_2 uptake kinetics ($\tau \cdot \dot{V}(\text{sub O}_2)$) during successive square-wave on-transients from loadless cycling to moderate exercise. We hypothesized that with a slow heart rate response (and O_2 transport limitation) O_2 kinetics would be slowed but that with a repeated exercise initiated while the heart rate remained elevated the $\tau \cdot \dot{V}(\text{sub O}_2)$ would be faster. Six male HT patients performed two ramp-function tests to determine peak O_2 uptake and ventilation threshold. Patients subsequently completed two repeats of a square-wave forcing function and repeated this on 2 days. Alveolar gas exchange was measured breath by breath. A monoexponential fit of signal-averaged data of the first exercise on-transient (between days) yielded a significantly slower $\tau \cdot \dot{V}(\text{sub O}_2)$ in HT subjects than in healthy men. With successive exercise (2nd transition) initiated while HR remained elevated the $\tau \cdot \dot{V}(\text{sub O}_2)$ of HT patients was 46 ± 17 s. The faster O_2 kinetics of the second transition suggests that O_2 delivery was enhanced and therefore that the $\tau \cdot \dot{V}(\text{sub O}_2)$ may reflect bioenergetic processes controlling the rate of oxidative metabolism. Author (Hemer)

A95-74373**INCREASED PEAK OXYGEN CONSUMPTION OF TRAINED MUSCLE REQUIRES INCREASED ELECTRON FLUX CAPACITY**

DEAN M. ROBINSON, ROBERT W. OGILVIE, PETER C. TULLSON, and RONALD L. TERJUNG *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1941-1952 (Contract(s)/Grant(s): NIH-HL-37387; NIH-AR-21617) (HTN-95-A0672) Copyright

The importance of the training-induced increase in mitochondrial capacity in realizing the increase in maximal O₂ consumption (dot-V(sub O₂ max)) of trained muscle was evaluated using an isolated perfused rat hindlimb preparation at a high blood flow during tetanic contractions. Rats trained for 8 - 12 wk by treadmill running exhibited an approximately 25% increase in muscle dot-V(sub O₂ max), an increase in mitochondrial enzyme activity, and an increase in tissue capillary (14%) that is expected to increase the O₂ exchange capacity of the tissue. Muscle dot-V(sub O₂ max) of sedentary and trained animals was determined, and electron transport capacity was acutely managed with myxothiazol, a tight-binding inhibitor of complex III. Inhibition of complex III was similar among (1) the low- and high-oxidation fibers and (2) the superficial and deep mitochondrial populations within muscle. Inhibition of NADH cytochrome-c reductase activity resulted in reductions in muscle dot-V(sub O₂ max) with similar dose responses (mean effective dose of approx. 0.2 micro M of myxothiazol added to the perfusion medium. The extraction of O₂ by the contracting muscle decreased as dot-V(sub O₂ max) declined. The increase in muscle dot-V(sub O₂ max) observed in the muscle of trained animals was eliminated when its electron transport capacity was reduced to that observed in normal sedentary rat muscle. Thus, the exercise-induced adaptation of an increased muscle mitochondrial content appears to be essential for trained muscle to exhibit its increased O₂ flux capacity. The results of the present experiment illustrate the importance of mitochondrial adaptations in muscle remodeled by exercise training.

Author (Herner)

A95-74374**LUNG PARENCHYMA AND TYPE 2 CELL MORPHOMETRICS: EFFECT OF SURFACTANT TREATMENT ON PRETERM VENTILATED LAMB LUNGS**

KENT E. PINKERTON, JAMES F. LEWIS, EVELYN D. RIDER, JANICE PEAKE, WAYNEA CHEN, AMY K. MADL, RICHARD H. LUU, MACHIKO Ikegami, and ALAN H. JOBE *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1953-1960

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The effect of exogenous surfactant treatment on lung and type II cell structure of ventilated lambs of 137 - 138 days gestational age was studied. Thirty-four lambs were delivered and randomized to control or 100 mg/kg of natural sheep surfactant treatment groups. Lungs from one group of lambs not treated with surfactant were fixed before ventilation, and the other animals were ventilated to maintain normal blood gas values for 3, 24, or 48 h. Morphometric assessment of the inflation-fixed lung parenchyma of ventilated lungs was compared with the architectural appearance of alveoli and alveolar ducts in the unventilated lungs. Mechanical ventilation resulted in distension of alveolar ducts accompanied by the shallowing and loss of well-defined alveoli and areas of atelectasis at 3 h. These abnormalities increased in severity after 24 and 48 h of ventilation. Surfactant treatment before ventilation significantly reduced the extent and degree of dilatation and concomitant atelectasis. The fraction of normal parenchyma was 38 +/- 7% in untreated lambs vs. 64 +/- in treated lambs after 24 h of ventilation. After 48 h of ventilation, significant differences between control (39 +/- 6%) and surfactant-treated (55 +/- 6%) lambs were still evident. Alveolar type II cells contained approximately 15% lamellar bodies by volume. Neither surfactant treatment nor time of ventilation altered the volume density of lamellar bodies or other organelles, except for a decrease in glycogen from 8% in nonventilated lungs to 2.5% in lungs ventilated for 24 h. These findings indicate that a surfactant treatment at birth results in the maintenance of more

normal parenchyma with less atelectasis during prolonged ventilation of the immature lung. There were no adverse effects of surfactant treatment on type II cells.

Author (Herner)

A95-74375**FATIGUE OF RAPID AND SLOW ONSET IN ISOLATED PERFUSED RAT AND MOUSE DIAPHRAGMS**

RALPH C. KOLBECK Medical Coll. of Georgia, Augusta, GA, US and THOMAS M. NOSEK Medical Coll. of Georgia, Augusta, GA, US *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1991-1998 Research sponsored by American Lung Association of Georgia

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Muscle fatigue was studied in the isolated perfused rat (66% oxidative fibers) and mouse (99% oxidative fibers) diaphragms. Both muscles displayed two fatigue patterns when exposed to 333-ms trains of 20-Hz stimulation. A rapid fatigue pattern appeared within each contractile train as an immediate progressive twitch-by-twitch diminution in contractility (a decrease in maximal isometric twitch tension (T) and maximal rate of T development). An intertrain slow fatigue pattern also appeared as a progressive train-by-train diminution in contractility and an increased maximal rate of relaxation normalized to T. A reduction in the stimulatory frequency from 20 to 2 Hz caused a considerable diminution in the rapid fatigue pattern. These data suggest that rapid fatigue results from the time course of mechanical restitution, the time necessary for the Ca(2+) channels of the sarcoplasmic reticulum to recover from inactivation. The slow fatigue pattern, on the other hand, is thought to be due to changes in the intracellular milieu. The difference in sensitivity of the rat and mouse diaphragms to rapid and slow fatigue is apparently related to differences in their fiber type composition. Thus, as would be expected, the mouse diaphragm, composed of only oxidative fibers, is less susceptible to slow fatigue compared with the rat diaphragm. On the other hand, it is more susceptible to rapid fatigue.

Author (Herner)

A95-74376**ATRIAL SEPTAL DEFECT BLUNTS THE IMPAIRMENT OF LEFT VENTRICULAR FUNCTION DURING THE MUELLER MANEUVER**

JUHA VIROLAINEN Helsinki Univ. Central Hospital, Helsinki, Finland, MARKKU VENTILA Helsinki Univ. Central Hospital, Helsinki, Finland, and MARKKU KUPARI Helsinki Univ. Central Hospital, Helsinki, Finland *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1999-2004 Research sponsored by Finnish Foundation of Cardiovascular Research

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To investigate whether atrial septal defect (ASD) modifies the left ventricular (LV) hemodynamic response to a fall of intrathoracic pressure (Mueller maneuver), we studied 15 patients with an uncomplicated ASD and 16 healthy control subjects. LV function was measured by M-mode and Doppler echocardiography at rest and during the maneuver. Indicator-dilution technique was used to quantify the pulmonary-to-systemic flow ratio. During comparable changes of intrathoracic pressure, LV systolic function and filling diminished in both groups but patients with ASD showed smaller reductions in LV stroke dimension, peak diameter shortening rate, transmitral velocity-time integral, and cardiac output. The pulmonary-to-systemic flow ratio increased from 2.1 +/- 0.1 to 2.6 +/- 0.2 in the ASD group. In conclusion, LV function diminishes significantly in healthy persons during the Mueller maneuver. In patients with ASD, the changes are directionally similar but quantitatively smaller. An interatrial communication mitigates the impairment of LV function after an acute and sustained drop of intrathoracic pressure.

Author (Herner)

A95-74378**RATIOS AND REGRESSIONS IN BODY SIZE AND FUNCTION: A COMMENTARY**

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Univ., Los Angeles Medical Center, Torrance, CA, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 2015-2017 Research sponsored by American Lung Association (Contract(s)/Grant(s): NIH-HD-11907; HIH-RR-00425) (HTN-95-A0677) Copyright

Toth et al. found that the ratio of peak oxygen consumption ($\dot{V}(\text{sub O}_2)$) to fat-free mass (FFM) was greater in a group of men than in a group of women. They suggested that the ratio approach was inherently misleading in assessing cardiorespiratory fitness and recommended that regression-based approaches (e.g., analysis of covariance (ANCOVA)) should be used to compare any and all size-related variables in different groups of subjects. We believe that the spurious results suggested by Toth et al. have little to do with ratios per se; rather, problems may result from the inappropriate use of ratios, or any other analytic tool, used to compare physiological values in populations that differ in size or gender. Ratios of physiological function to body size have proven to be a convenient, often revealing, and useful first step in analyzing the underlying biology of size and function.

Author (revised by Herner)

A95-74379

EFFECT OF SAMPLING SITE ON FEMORAL VENOUS BLOOD GAS VALUES

ALVAR G. N. AGUSTI, JOSEP ROCA, JOAN A. BARBERA, JORDI CASADEMONT, ROBERT RODRIGUEX-ROISIN, and PETER D. WAGNER Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 2018-2022 Research sponsored by Direccio General de l'Esport de la Generalitat de Catalunya and California Univ.

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To examine whether the tip of the femoral vein catheter used for sampling femoral venous $P(\text{sub O}_2)$ during cycling exercise is contaminated by skin or saphenous vein blood, we studied 6 healthy volunteers during three identical incremental exercise tests while breathing room air on the same day. Femoral venous blood was sampled simultaneously from two catheters inserted into the femoral vein but advanced in opposite directions (7 cm distally and 5 cm proximally). Blood sampling for measurements of $P(\text{sub O}_2)$, $P(\text{sub CO}_2)$, pH, hemoglobin concentration, and oxyhemoglobin saturation was done simultaneously from both catheters in duplicate at rest, at 60% of maximum workload (60% W), and at maximum symptom-limited exercise (100% W). Temperature was measured with a thermistor probe placed in the proximal catheter. At rest, distal $P(\text{sub O}_2)$ was significantly lower than that measured proximally, but no differences were found during exercise. Comparison of blood temperatures between proximal and distal sites of sampling in two subjects showed negligible differences. Intrasubject coefficient of variation of distal femoral venous $P(\text{sub O}_2)$ over the three bouts of exercise was 11.5% at rest, 5.9% at 60% W, and 5.6% at 100% W. Mean differences in distal $P(\text{sub O}_2)$ between duplicate samples were 0.5 ± 1.4 mmHg at rest, 0.1 ± 0.8 mmHg at 60% W, and 0.6 ± 0.9 mmHg at 100% W. We conclude that the site of femoral venous sampling may influence the analysis of muscle O_2 transport at rest but not at equal to or greater than 60% maximal O_2 uptake, suggesting negligible contributions to O_2 indexes from nonexercising tissues under these conditions.

Author (Herner)

A95-74380

EVALUATION OF DYNAMIC RESPONSE OF CATHETER-MANOMETER SYSTEMS FOR PULMONARY ARTERIAL PRESSURE

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To quantitatively evaluate the waveform distortions observed through a catheter-manometer system, the tolerance range of amplitude errors and that of phase errors are defined as both within $\pm 5\%$, and the frequency bandwidth was calculated where the frequency characteristics of amplitude and those of phase difference satisfy the two tolerance ranges by use of a second-order kinetic equation. The results were expressed by three variables, composed of the natural frequency ($f(\text{sub n})$), damping coefficient (zeta), and highest frequency ($f(\text{sub h})$) corresponding to the frequency bandwidth; a chart was constructed with $f(\text{sub n})$ on the x-axis, zeta on the y-axis, and $f(\text{sub h})$ as parameter. Also on the chart, the propagation delay times ($t(\text{sub d})$'s) determined by $f(\text{sub n})$, zeta, and $f(\text{sub h})$ were plotted. We measured the frequency characteristics of two 7-Fr Swan-Ganz catheters with lengths of 75 and 110 cm. $f(\text{sub n})$'s and zeta's were found to be 13.9 and 10.1 Hz and 0.23 and 0.32, respectively. Referring to this chart, the maximal $f(\text{sub h})$ these catheters would be able to reproduce within the tolerance ranges and the propagation $t(\text{sub d})$'s can be predicted to be 3.2 and 2.4 Hz and 7 and 12 ms, respectively. Suppression of resonance by use of Accudynamic improved the maximal $f(\text{sub h})$'s to 3.9 and 2.9 Hz, respectively, but resulted in the increased $t(\text{sub d})$'s to 14 and 19 ms due to increased zeta.

Author (Herner)

A95-74381

STRUCTURAL COMPOSITION OF LUNG PARENCHYMAL STRIP AND MECHANICAL BEHAVIOR DURING SINUSOIDAL OSCILLATION

M. S. LUDWIG Royal Victoria Hospital, McGill Univ., Montreal, Canada and M. J. DALLAIRE Royal Victoria Hospital, McGill Univ., Montreal, Canada Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 2029-2035 Research sponsored by J. T. Costello Memorial Research Fund, Respiratory Health Network of Centres of Excellence, and Medical Research Council of Canada (HTN-95-A0680) Copyright

The lung parenchymal strip is comprised of many different anatomic elements, including small vessels, small airways, and alveolar walls. We questioned whether the relative amounts of these different structures are important in determining the mechanical behavior of this preparation during dynamic oscillations. We studied 16 parenchymal strips ($10 \times 2 \times 2$ mm) from 12 Sprague-Dawley rats. The strips were suspended in an organ bath filled with Krebs solution, bubbled with 95% O_2 - 5% CO_2 , and maintained at 37°C. One end of the strip was attached to a force transducer, and the other end was attached to a lever system that effected length (L) changes. We oscillated the strips at various resting tensions (T) (0.9 and 1.5 g), frequencies (0.1, 0.3, 0.6, and 1.0 Hz), and amplitudes (1.1, 2.4, and 5.3% of optimal L). We obtained T vs. L curves and calculated the resistance, elastance, and hysteresivity (ratio of energy dissipated to energy stored) of the tissue. At the end of the experiment, the strips were fixed in Formalin at $T = 1$ g. Histological sections were examined, and the amounts of airway, blood vessel, and alveolar wall were quantified using point counting techniques. We found that whereas resistance varies significantly with frequency and T, elastance and hysteresivity varies with only T. The fractional areas of alveolar, blood vessel, and bronchial wall were 86.3 ± 0.5 (SE), 8.4 ± 0.3 , and $5.3 \pm 0.4\%$. Only hysteresivity and the fractional area of alveolar wall were significantly correlated at the lower resting tension. We conclude that the long parenchymal strip is a sound model for examining the dynamic behavior of lung tissues.

Author (Herner)

A95-74382

ERGOMETRIC STUDIES OF UNTRAINED SKELETAL MUSCLE DEMONSTRATE FEASIBILITY OF MUSCLE-POWERED CARDIAC ASSISTANCE

DENNIS R. TRUMBLE Allegheny General Hospital, Pittsburgh, PA, US and JAMES A. MAGOVERN Medical Coll. of Pennsylvania, Pittsburgh, PA, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 2036-2041

51 LIFE SCIENCES (GENERAL)

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The feasibility of biomechanical circulatory assistance hinges on the capacity of skeletal muscle to generate significant hemodynamic work. This study quantifies linear contractile energetics via a customized hydraulic ergometer. Six normal canine latissimus dorsi (LD) muscles (200 \pm 25 g) were evaluated. The muscles were not mobilized; thereby their collateral circulation was preserved. The humeral insertion of the LD muscle was transected and connected to the ergometer. Preload was adjusted to return the LD muscle to its in situ length, and one pulse train was delivered every second. The resulting contractions generated peak pressures of 134 \pm 17 mmHg with mean pressures during shortening of 102 \pm 12 mmHg. Flow rates averaged 5.45 \pm 0.26 l/min. Mechanical work output was calculated at 1.14 \pm 0.18 J/contraction, yielding an average power production of 4.57 \pm 0.72 W during shortening. Continuous LD output power, measured at 5.76 \pm 0.90 mW/g, compares favorably with the 3.48 mW/g typically generated by a 350-g human heart. We therefore conclude that skeletal muscle of sufficient mass can sustain work rates suitable for cardiac assistance despite the 50% power losses typically experienced after muscle training.

Author (Hemer)

A95-74383

A SIMPLE HANDHELD PUSH-BUTTON DEVICE FOR IN SITU CALIBRATION OF PNEUMOTACHOGRAPHS

WIM P. J. HOLLAND, WIM BOENDER, JOOP A. T. BOS, and PAUL E. M. HUYGEN *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 2042-2047

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A simple and compact flow calibrator has been devised for generating precise predetermined constant flow rates for checking the calibration of laboratory and clinical flow transducers used in respiratory measurements. The standard version delivers preset flows of 0.5 and 1 l/s, whereas a tuned-up version can produce preset flows of 2.5 and 5 l/s, with an accuracy of \pm 2%. The pressure generated is sufficient to cope with most commonly used respiratory flowmeters. The flow calibrator is built from inexpensive components that are readily obtainable: a fan, a turbine flowmeter, and a feedback circuit in a compact housing. The device is easy to connect to other equipment and to operate. Three flow calibrators have been built and are in regular use in a lung function laboratory and on intensive care wards.

Author (Hemer)

A95-75252

METABOLIC AND VENTILATORY RESPONSES TO ANEMIC HYPOXIA IN CONSCIOUS RATS

TAKAFUMI MATSUOKA McGill Univ., Montreal, Canada, CHIKAKO SAIKI McGill Univ., Montreal, Canada, and JACOPO P. MORTOLA McGill Univ., Montreal, Canada *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1067-1072

Research sponsored by Medical Research Council of Canada and Quebec Lung Association

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We investigated the metabolic and ventilatory effects of anemia, which is characterized by a decrease in blood O₂ content with no changes in arterial PO₂ (Pa(sub O₂)). Anemia was obtained in conscious chronically instrumented adult male rats by substituting blood with equal volumes of Ringer lactate solution via the tail artery. Three hours later, we measured resting O₂ consumption (dot-VO₂) by an open flow method and ventilation (dot-VE) by the barometric method. Hemodilution to 80 - 90, 70 - 80, or 60 - 70% of the starting hematocrit and hemoglobin values had no major effects on dot-VO₂, dot-VE, or mean arterial blood pressure (MAP). A 50 - 60% hemodilution reduced dot-VO₂ and MAP, with a modest increase in dot-VE, the rats were hypocapnic, with normal Pa(sub O₂). Infusion of vasopressin in a dosage sufficient to increase MAP to the basal value resulted in a reduction in dot-VE, a further drop in dot-VO₂, and a return to normocapnia. Three days after hemodilution, hematocrit and hemoglobin were still low but ventilatory and metabolic parameters were normal. In conclusion, in this rat model of anemic

hypoxia, (1) hypometabolism occurred without a drop in Pa(sub O₂), implying that its manifestation does not require activation of the carotid body, and (2) the transient hypocapnia resulted from the dot-VE stimulating effects of the hypotension.

Author (Hemer)

A95-75253

CEREBELLAR MODULATION OF VENTILATORY RESPONSE TO PROGRESSIVE HYPERCAPNIA

FADI XU Kentucky Univ., Lexington, KY, US, JAMES OWEN Kentucky Univ., Lexington, KY, US, and DONALD T. FRAZIER Kentucky Univ., Lexington, KY, US *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1073-1080

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The cerebellar contribution to the ventilatory response to progressive hypercapnia was examined in 18 anesthetized tracheotomized spontaneously breathing cats. The absolute values for minute ventilation (dot-VE), tidal volume (VT), respiratory frequency (f), inspiratory duty cycle (Ti/TT), and mean inspiratory flow (VT/Ti) were measured. Progressive hypercapnia was induced using the rebreathing method. The respiratory variables at each level of PET(sub CO₂) and the slopes of ventilatory (VT and f) responses to hypercapnia were compared across the intact, decerebellate, and decerebellate-vagotomized preparations. In 12 cats, decerebellation preceded vagotomy, and in 6 cats the order of the surgical procedures was reversed. The results show that, compared with intact control, decerebellation had little effect on respiratory variables when PET(sub CO₂) was 30 - 35 Torr. However, during a hypercapnic challenge, dot-VE and the slope of the dot-VE response were significantly reduced. Bilateral vagotomy increased VT and decreased f but failed to alter the ventilatory response in the PET(sub CO₂) range of 35 - 55 Torr. However, combination of decerebellation and vagotomy, regardless of the surgical order, severely blunted dot-VE and the slopes of dot-VE, VT, and f responses. When decerebellation followed vagotomy, significant decreases in VT (absolute values and slopes) were noted with little further alteration in f response. We conclude that the cerebellum and its interaction with the vagus nerves play a facilitatory or disinhibitory role in the ventilatory responses to hypercapnia.

Author (Hemer)

A95-75254

PROTEIN ACCUMULATION IN CEREBROSPINAL FLUID DURING -90 DEG HEAD-DOWN TILT IN RABBIT

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Plasma proteins are only somewhat larger than the intercellular spaces of the cerebral microvessels that constitute the blood-brain barrier or of the choroid plexus villi that elaborate cerebrospinal fluid (CSF). We hypothesized that the integrity of these barriers in anesthetized rabbits might be compromised during head-down tilt (HDT). Plasma protein and osmolality, hematocrit, and CSF protein concentration were compared in rabbits exposed to 1 h of HDT and prone rabbits. In addition, the concentration of trypan blue dye, injected intravenously at the end of HDT or the prone position, was measured in brain homogenate. Finally, arterial blood pressure was measured via a catheterized carotid artery. HDT disrupted the barrier between blood and CSF, as indicated by a significantly greater brain trypan blue concentration in the HDT rabbits than in the prone rabbits. Moreover, CSF protein 5 min after HDT onset was significantly increased compared with control in HDT rabbits but not in prone rabbits. Changes in the plasma protein-to-hematocrit ratio in the HDT animals, but not in the prone animals, were also compatible with a loss of fluid from the vascular compartment. Because arterial blood pressure was elevated in the HDT compared

with the prone rabbits, it appears likely that the intercellular spaces of the cerebral microvessels and/or choroid plexus widened as a result of the acute hypertension, permitting the leakage of protein from blood to brain.
Author (Hemer)

A95-75255

EFFECTS OF RESISTANCE EXERCISE ON GLUCOSE TOLERANCE IN NORMAL AND GLUCOSE-INTOLERANT SUBJECTS

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This study was conducted to determine whether improvements in glucose tolerance could be observed after a single bout of resistance exercise in young control subjects, older patients with non-insulin-dependent diabetes mellitus (NIDDM), and older age-matched control subjects. Each subject was screened for fitness level and any contraindications to exercise before inclusion in the study. A 75-g oral glucose tolerance test was administered 2 wk after the subjects were screened, and the subjects were familiarized with the exercise equipment. The maximum weight that could be lifted with one repetition was determined on seven Nautilus machines that utilized the upper and lower body. After a 48-h rest period, a 3-set x 10-repetition protocol based on the subject's one repetition maximum was completed by each participant on each machine. Eighteen hours after the lifting protocol, a second oral glucose tolerance test was administered. There was no change in the pre- to post-exercise glucose levels in any of the treatment groups, but the total insulin responses (area under the curve) of the young control and NIDDM groups were significantly lower after exercise. The postexercise C-peptide levels were unchanged in all groups. The decrease in insulin 18 h after exercise in the young control and NIDDM groups, with no change in insulin secretion (C-peptide data), indicates an enhanced ability to clear insulin from the blood. Whether the removal is peripheral and/or hepatic cannot be determined from these data, but the results show that resistance exercise can influence insulin action without affecting glucose tolerance.
Author (Hemer)

A95-75256

PATHOLOGICAL O₂ SUPPLY DEPENDENCE OF DIAPHRAGMATIC AND SYSTEMIC O₂ UPTAKE DURING ENDOTOXEMIA

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Our aim was to assess whether endotoxemia impairs the ability of the diaphragm to extract O₂ and whether this defect leads to a greater dependence of O₂ uptake on O₂ delivery. In two groups of anesthetized mechanically ventilated dogs, the left hemidiaphragm was vascularly isolated. Diaphragmatic blood flow and cardiac output (CO) were measured simultaneously in all animals. Saline (S group) or *Escherichia coli* endotoxin (100 mg; E group) was infused intravenously over 60 min. In both groups, CO was reduced in stages by controlled hemorrhage, and systemic and diaphragmatic O₂ deliveries and consumptions were measured at each stage to construct the O₂ delivery - O₂ consumption relationships. In the S group, the average systemic O₂ delivery below which O₂ uptake became supply dependent was 7.2 ml/kg/min. At this O₂ delivery, systemic O₂ extraction ratio (ER) averaged 67.9%, whereas the maximum O₂ ER was 91.3%. Critical diaphragmatic O₂ delivery and critical and maximum diaphragmatic O₂ ER, by comparison, averaged 9.0 ml/kg/min, 65%, and 81.9%, respectively. Endotoxin infusion raised critical systemic O₂ delivery to 16.7 ml/kg/min and reduced critical and maximum systemic O₂ ER to 55.5 and 77%, respec-

tively. Similarly, critical diaphragmatic O₂ delivery in the E group increased to 14.8 ml/kg/min, whereas critical and maximum O₂ ER declined to 51.8 and 72.8%, respectively. Thus, endotoxemia impairs diaphragmatic O₂ extraction. This, in turn, leads to a greater dependence of diaphragmatic O₂ uptake on O₂ delivery.
Author (Hemer)

A95-75257

FUNCTIONAL AND STRUCTURAL CHANGES WITH HYPOXIA IN PULMONARY CIRCULATION OF SPONTANEOUSLY HYPERTENSIVE RATS

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Chronic hypoxic pulmonary hypertension involves both vasoconstriction and vascular remodeling. Spontaneously hypertensive rats (SHR) have an increased systemic vascular resistance and a greater responsiveness to constricting stimuli. We hypothesized that, in contrast to age-matched normotensive Wistar-Kyoto rats (WKY), SHR also display spontaneous pulmonary hypertension in normoxia and increased vascular response to acute and chronic hypoxia. Baseline mean pulmonary arterial pressure (PAP) and total pulmonary resistance (TPR) were higher in SHR than in WKY. With acute hypoxia (10% O₂ for 15 min), PAP increased to the same extent in SHR and WKY and cardiac output (CO) was unchanged in WKY but increased in SHR. Thus, the rise in PAP in the SHR might be accounted for by the rise in CO, as TPR did not rise, but not that in the WKY, as TPR increased. After 12 days in hypoxia (10% O₂), mean arterial pressure was unchanged in WKY but decreased significantly in SHR without a change in CO. PAP increased by 59% in SHR and 54% in WKY when the rats were taken from the hypoxic chamber for 1 h. Acute hypoxic challenge caused a further increase in PAP only in WKY. Medial wall thickness of alveolar duct and terminal bronchial vessels was similar in WKY and SHR after chronic hypoxia. We conclude that SHR exhibit mild baseline pulmonary hypertension in normoxia and that chronic hypoxia does not produce a disproportionate increase in SHR pulmonary vascular remodeling and pulmonary hypertension.
Author (Hemer)

A95-75258

DIETARY EFFECTS ON EXERCISING MUSCLE METABOLISM AND PERFORMANCE BY P-31-MRS

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To determine how diet modulates short-term exercise capacity, skeletal muscle pH and bioenergetic state were examined by P-31-magnetic resonance spectroscopy in nine healthy volunteers. Subjects performed incremental quadriceps exercise to exhaustion after 5 days of high-carbohydrate (HCHO) or high-fat (HFAT) diet randomly assigned in crossover fashion and separated by a 2.5-day period of ad libitum mixed diet. Simultaneous measurements were made of pulmonary gas exchange, minute ventilation, and quadriceps muscle pH and phosphorylation potential. At rest and peak exercise, respiratory exchange ratio and minute ventilation were higher after HCHO than after HFAT, reflecting greater CHO utilization. Peak O₂ consumption (dot-V(sub O₂)) was not increased after HCHO, but exercise duration was. HCHO was associated with a blunted early fall of phosphocreatine (PCr)/P(sub i) vs. dot-V(sub O₂). On both study days, the slope of PCr/P(sub i) vs. dot-V(sub O₂), before and after the PCr threshold, was correlated with exercise time. The results suggest that a diet rich in CHO improves exercise efficiency through beneficial effects on intracellular phosphorylation potential.
Author (revised by Hemer)

A95-75259

VASCULAR PERMEABILITY AND EPITHELIAL TRANSPORT EFFECTS ON LUNG EDEMA FORMATION IN ISCHEMIA AND REPERFUSION

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To determine the role of various Na(+) transport systems in the edema fluid accumulation after ischemia and reperfusion in the lung, we evaluated the effect of amiloride (a Na(+) channel blocker), ouabain (a Na(+)-K(+)-adenosinetriphosphatase blocker), and phloridzin (a Na(+)-glucose cotransport blocker) in isolated rat lungs. Ischemia and reperfusion (I/R) significantly increased the edema accumulation, with the wet-to-dry weight ratios increasing to 10.14 \pm 0.58 from 6.03 \pm 0.05 in control lungs. Amiloride significantly augmented the amount of edema fluid (wet-to-dry weight ratio 12.26 \pm 0.77), and ouabain further increased the amount of edema (wet-to-dry weight ratio 18.58 \pm 1.00). Phloridzin did not significantly affect edema formation associated with I/R. Isoproterenol decreased the amount of edema formation in the presence and absence of amiloride. This occurred because the endothelial permeability as assessed by filtration coefficient was restored to normal values and less edema formed. The present study indicates that Na(+) channels and Na(+)-K(+)-adenosinetriphosphatase, components of the active Na(+) absorption transport system, are very important in opposing edema fluid accumulation in rat lungs subjected to I/R injury and operate as an edema safety factor. However, if the endothelial damage associated with I/R is allowed to persist, then the transport processes, even if operative, are insufficient to prevent continuous edema accumulation.

Author (Hemer)

A95-75260

STRENGTH TRAINING INCREASES INSULIN ACTION IN HEALTHY 50- TO 65-YR-OLD MEN

JOHN P. MILLER, RICHARD E. PRATLEY, ANDREW P. GOLDBERG, PATRICIA GORDON, MICHELLE RUBIN, MARAGARITA S. TREUTH, ALICE S. RYAN, and BEN F. HURLEY *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1122-1127

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The insulin resistance associated with aging may be due, in part, to reduced levels of physical activity in the elderly. We hypothesized that strength training increases insulin action in older individuals. To test this hypothesis, 11 healthy men 50 - 63 yr old underwent a two-step hyperinsulinemic-euglycemic glucose clamp with concurrent indirect calorimetry and an oral glucose tolerance test (OGTT) before and after 16 wk of strength training. The training program increased overall strength by 47%. Fat-free mass (FFM; measured by hydrodensitometry) increased and body fat decreased with training. Fasting plasma glucose levels and glucose levels during the OGTT were not significantly lower after training. In contrast, fasting plasma insulin levels decreased and insulin levels decreased during the OGTT. Glucose infusion rates during the hyperinsulinemic-euglycemic glucose clamp increased 24% during the low insulin infusion and increased 22% during the high insulin infusion. These increases were accompanied by a 40% increase in nonoxidative glucose metabolism during the high insulin infusion. These results demonstrate that strength training increases insulin action and lowers plasma insulin levels in middle-aged and older men.

Author (revised by Hemer)

A95-75261

CHANGES IN SATELLITE CELL MITOTIC ACTIVITY DURING ACUTE PERIOD OF UNILATERAL DIAPHRAGM DENERVATION

LUC E. GOSSELIN, GLENN BRICE, BRETT CARLSON, Y. S. PRAKASH, and GARY C. SIECK *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1128-1134 (Contract(s)/Grant(s): NIH-HL-34817; NIH-HL-37680)

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The acute period of unilateral diaphragm denervation (DNV) is associated with increases in cell mitotic activity, protein synthesis, and muscle fiber hypertrophy. Our purpose was to determine whether acute unilateral diaphragm DNV is associated with changes in muscle isometric contractile properties, cross-sectional area of different muscle fiber types, mitotic activity of muscle satellite cells, and muscle fiber ultrastructural properties indicative of injury. Adult male Fischer 344 rats underwent a right phrenicotomy, and DNV and intact (INT) hemidiaphragms were studied 72 h later. DNV hemidiaphragm displayed a significant decline in maximal isometric force and a prolonged time to peak twitch force and time to half relaxation compared with INT contralateral hemidiaphragm. DNV resulted in a significant increase in cross-sectional area of types I (33%), IIa (35%), and IIb (28%) fibers relative to INT hemidiaphragm. Satellite cell mitotic activity (assessed by incorporation of bromodeoxyuridine) was approximately 5.5 times greater in DNV than in INT muscle. Ultrastructural examination of electron micrographs revealed alterations in Z-line and sarcomeric structure indicative of muscle injury. Cellular infiltration and segmental necrosis were also noted in some fibers. We conclude that acute unilateral diaphragm DNV results in muscle fiber injury that induces satellite cell activation. We also speculate that the specific force decrement associated with DNV is at least partially the result of muscle injury.

Author (revised by Hemer)

A95-75262

EFFECTS OF LENGTH AND STIMULATION FREQUENCY ON FATIGUE OF THE HUMAN TIBIALIS ANTERIOR MUSCLE

P. SACCO University Coll. London, London, UK, D. B. MCINTYRE University Coll. London, London, UK, and D. A. JONES University Coll. London, London, UK *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1148-1154

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It has been suggested that the reduced fatigability of muscles exercised at short length may result from a decrease in the metabolic cost of contractions in the shortened position. We compared the fatigue properties and metabolic cost of stimulated isometric tetanic contractions in the tibialis anterior of 10 normal subjects at the optimum length (L(sub O)) for force production and when the muscle was shortened (L(sub S)). Six 15-s isometric contractions at L(sub S) caused force to decline to 53% of the fresh value when tested at L(sub O), whereas muscles exercised and tested at L(sub O) declined to 40% of fresh force. However, the extent of fatigue was proportionately greater if the muscle was exercised and tested at L(sub S). The apparent fatigue resistance of short muscles was found to be a consequence of recovery occurring under ischemic conditions while the muscle was changed from L(sub S) to L(sub O). P-31-nuclear magnetic resonance spectroscopy showed similar metabolic changes associated with 5-s stimulated contractions at L(sub O) and L(sub S), indicating that any differences in fatigability at the two lengths were not caused by altered metabolic costs. The similarity between the force profiles of muscles fatigued at L(sub S) and those fatigued by high-frequency stimulation supports the hypothesis that an enhanced activation failure occurs at L(sub S), possibly resulting from failure of sarcolemmal action potential propagation in the transverse tubules.

Author (Hemer)

A95-75263

EDEMA DEVELOPMENT AND RECOVERY IN NEUROGENIC PULMONARY EDEMA

MICHAEL B. MARON, PAUL H. HOLCOMB, CHRISTOPHER A. DAWSON, DAVID A. RICKABY, ANNE V. CLOUGH, and JOHN H.

LINEHAN Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1155-1163 Research sponsored by Dept. of Veterans Affairs (Contract(s)/Grant(s): NIH-HL-31070; NIH-HL-24349) (HTN-95-A0694) Copyright

We determined the time course of changes in extravascular lung water (EVLW) that occur after massive sympathetic activation produced by intracisternal veratrine administration in chloralose-anesthetized dogs. Three groups were studied. In the first group, acute increases in EVLW (occurring within minutes) were determined both by measuring extravascular thermal volume and by gravimetric analysis. In the second and third groups, changes in EVLW were followed for 2 - 3 h after veratrine administration. Extravascular thermal volume was measured in the second group. In the third group, right atrial injections of a vascular indicator (I-125-labeled serum albumin) and an extravascular indicator ((3) HOH) were made while blood was sampled from the pulmonary artery (PA) and left atrium, and EVLW was determined by deconvolution of the left atrial and PA concentration-time curves. Indicator-dilution and gravimetric EVLW increased acutely only in dogs in which PA pressure exceeded 60 Torr, with two- to four-fold increases in EVLW being observed in dogs that developed the highest PA pressures (maximum 94 Torr). Thus, severe edema can develop rapidly after massive sympathetic nervous system activation but requires extreme degrees of pulmonary hypertension. In several dogs after the acute increase in EVLW associated with the pulmonary hypertension, the indicator-dilution EVLW decreased with time. These decreases appear to reflect clearance of edema fluid rather than alterations in perfusion. Author (Herner)

A95-75264

INTERACTIVE EFFECTS OF K(+), ACIDOSIS, AND CATECHOLAMINES ON ISOLATED RABBIT HEART; IMPLICATIONS FOR EXERCISE

STEWART P. LEITCH University Lab. of Physiology, Oxford, UK and DAVID J. PATERSON University Lab. of Physiology, Oxford, UK Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1164-1171 Research sponsored by Wellcome Trust, Royal Society, and British Heart Foundation (HTN-95-A0695) Copyright

Intense exercise can double arterial K(+) concentration, decrease pH by 0.4 units, and increase catecholamines 15-fold. Any one of these changes may be cardiotoxic in a subject at rest, yet these changes are well tolerated in exercise. We tested the interactive effects of extracellular K(+) concentration, metabolic acidosis (pH 7.0), and raised catecholamines in the isolated working rabbit heart when they were changed with similar kinetics and concentrations to those seen in exercise. Raised extracellular K(+) concentration (8 and 12 mM) significantly decreased aortic flow (AF) by 23 and 76%, respectively. Acidosis decreased AF by 19% and by 38% in combination with 8 mM extracellular K(+) concentration, making their combined effect additive. Either epinephrine (80 nM), norepinephrine (80 nM) or extracellular Ca(2+) concentration (5 mM) offset the negative effects of 8 and 12 mM extracellular K(+) concentration on AF. Norepinephrine also improved AF in 8 mM extracellular K(+) concentration with acidosis. Thus, there may be a beneficial interaction among changes in K(+), catecholamines, and acidosis during exercise such that each could offset the others' potentially harmful effects. Author (Herner)

A95-75265

EFFECTS OF SOLUTION OSMOLALITY ON ABSORPTION OF SELECT FLUID REPLACEMENT SOLUTIONS IN HUMAN DUODENOJEJUNUM

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These experiments examined relationships between of an initial osmolality and carbohydrate (CHO) composition of an infused solution and osmolality and water and CHO absorption in a test segment. A triple-lumen tube with a 10-cm mixing segment and a 40-cm test segment was passed into the duodenojejunum. The infusion port was approximately 10 cm beyond the pyloric sphincter. Perfusion solutions were hypotonic (186 mosmol/kg; solution A), isotonic (283 mosmol/kg; solution B), and hypertonic (403 mosmol/kg; solution C). All solutions contained 18 meq Na(+) and 3 meq K(+). In the mixing segment, osmolality increased 83 mosmol/kg and decreased 90 mosmol/kg for solutions A and C, respectively. Corresponding changes in the test segment were an increase of 60 mosmol/kg and a decrease of 34 mosmol/kg. The osmolality of solution B did not change. In the test segment, mean osmolality and water and total solute fluxes were not significantly different among solutions, but solution C produced 27% greater fluid absorption than did solution A. When net fluid movement from mixing and test segments was determined, solution A produced 17% greater fluid absorption than did solution C. The mean increases in plasma and urine volumes over the 80-min test period were not significantly different. In the test segment, water flux correlated with CHO and Na(+) fluxes but not with osmolality. In conclusion, (1) significant differences in solution osmolality were eliminated within the proximal duodenum and (2) perfusing 6% CHO solutions with osmolalities ranging from 186 to 403 mosmol/kg did not produce significant differences in fluid homeostasis (plasma volume) at the end of an 80-min test period. Author (Herner)

A95-75266* National Aeronautics and Space Administration. Ames Research Center, Moffett Field, CA.

INTERACTION OF CHRONIC REATINE DEPLETION AND MUSCLE UNLOADING EFFECTS ON POSTURAL AND LOCOMOTOR MUSCLES

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In this study, creatine depletion was induced separately and in combination with non-weight-bearing activity to determine if the response to lowering this metabolite would counter the MHC transitions expected from non-weight-bearing. Creatine depletion was induced by feeding rats a diet supplemented with the creatine analogue beta-guanidinopropionic acid (beta-GPA). Animals were fed a diet containing the creatine analogue for 68 days. Hindlimb non-weight-bearing in BS and NS animals was accomplished by tail suspension for the final 30 days of this period. Beta-GPA feeding lowered the creatine content of muscles sampled by 65%. Creatine depletion resulted in a 16% increase in citrate synthase activity in the soleus (SOL) and a 24% increase in the plantaris (PLN). In two postural muscles, the SOL and vastus intermedius (VI), tail suspension resulted in large decreases in the type I MHC expression and increases in type IIx and IIb MHCs. In two locomotor muscles, the PLN and medial gastrocnemius, type I MHC declined and type IIb increased with suspension. Creatine depletion did not prevent the suspension-induced decline in type I MHC in any of these muscles. The increase in type IIb MHC was either prevented or reduced by creatine depletion before and during suspension in the SOL, VI, and PLN. Creatine depletion alone resulted in small increases in type I and IIa MHCs in the two locomotor muscles, but it had no effect on the MHC profile of the postural muscles studied. These results indicate that the mechanical signal generated by the hindlimb non-weight-bearing state dominated over the metabolic stimulus of creatine depletion with respect to the primary adaptation involving a reduction in type I MHC. Author (revised by Herner)

A95-75267

SYNTHETIC SURFACTANT SCAVENGES OXIDANTS AND PROTECTS AGAINST HYPEROXIC LUNG INJURY

ANDREW J. GHIO, PHILIP J. FRACICA, STEPHEN L. YOUNG, and CLAUDE A. PIANTADOSI *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1217-1223 (Contract(s)/Grant(s): NIH-HL-31992; NIH-HL-02655; NIH-HL-32188) (HTN-95-A0698) Copyright

Injury and mortality after exposure to 100% oxygen can be diminished by surfactants that may operate by mechanisms other than those responsible for surface tension effects. We tested the hypotheses that (1) synthetic surfactant and its components function as antioxidants in vitro and (2) decrements in hyperoxic injury after treatment with a surfactant and its components are associated with decreases in oxidative stress to the lung. A synthetic surfactant (Exosurf) and its non-surface-active components tyloxapol and cetyl alcohol were incubated in an iron-containing hydroxyl radical-generating system to determine their abilities to prevent oxidation of deoxyribose. Doses of tyloxapol, cetyl alcohol, and artificial surfactant diminished the absorbance of thiobarbituric acid-reactive products of deoxyribose. Similarly, tyloxapol, cetyl alcohol, and the surfactant decreased hydroxylated products of salicylate in the same system. Rats were instilled intratracheally with saline, tyloxapol, tyloxapol plus cetyl alcohol, or artificial surfactant and immediately exposed to air or 100% oxygen. After 61 h of oxygen exposure, pleural fluid volume and wet-to-dry lung weight ratios were decreased in animals treated with surfactant and/or its components. There were also decrements in thiobarbituric acid-reactive products of lung tissue. In separate experiments, mean survival of saline-treated rats exposed to 100% oxygen was 67.3 \pm 8.1 h and greater than 96 h for rats given the surfactant or its components. We conclude that tyloxapol, cetyl alcohol, and Exosurf can function as antioxidants in vitro and their in vivo instillation is associated with reduction in measures of hyperoxic injury, oxidized tissue products, and mortality.

Author (Hemer)

A95-75268

CEREBELLAR ROLE IN THE LOAD-COMPENSATING RESPONSE OF EXPIRATORY MUSCLE

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The hypothesis that the cerebellum is involved in the load-compensating response of expiratory muscles to expiratory tracheal occlusion was tested in anesthetized cats. A continuous expiratory threshold load (ETL; 5 cmH₂O) was applied to elicit consistent phasic baseline electromyographic activity in the transversus abdominis muscle (EMG(sub ab)). Tracheal occlusion for single expirations (TO(sub E)) were applied, and the evoked responses were compared in the intact and decerebellate preparation. Cold blockade of the dorsal spinal column and bilateral vagal inactivation (cold blockade or transection) were employed to determine the role of afferents from the lung, airways, chest wall, and diaphragm in shaping the cerebellar involvement in the motor response. The results showed that (1) decerebellation increased the baseline amplitude of the integrated EMG(sub ab) activity with little change in expiratory duration, (2) TO(sub E) applied after decerebellation markedly increased the expiratory duration compared with the intact values, (3) cooling the dorsal spinal columns (C5-7) did not significantly affect EMG(sub ab) response in the intact or decerebellate preparations, and (4) vagal inactivation in the intact or decerebellate preparation significantly eliminated the responses to ETL and TO(sub E). We conclude that the cerebellum is involved in the modulation of transversus abdominis activity during ETL and TO(sub E). Vagal afferents provide the major sensory input for the cerebellar modulation of the expiratory loading response.

Author (Hemer)

A95-75269

EFFECTS OF DETECTION AND CLASSIFICATION OF RESISTIVE AND ELASTIC LOADS ON ENDOGENOUS EVENT-RELATED POTENTIALS

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Resistive and elastic loads added to inspiration are readily detected, and detection latencies vary as a function of load magnitude and load type. In the present study, we recorded endogenous event-related potentials (i.e., N2 and P3) to the detection and classification of large and small loads equated for subjective magnitude in 14 men. In blocks of trials comprised of either large or small loads, subjects made a button-press response upon detecting a load and then classified the load as resistive or elastic. Loads were presented briefly early in inspiration and at the same level of inspiratory pressure. For loads of comparable magnitude, subjects detected equivalent numbers of resistive and elastic loads but could not discriminate reliability between load types. On the other hand, the latency of N2 was shorter to larger than to smaller loads, to resistive than to elastic loads, and to correct than to incorrect load classifications. The latency of P3 was affected similarly by load magnitude and load type. These findings demonstrate that event-related potentials are elicited by brief presentations of resistive and elastic loads and that N2 and P3 latencies vary reliably as a function of load magnitude and load type. Most importantly, event-related potential latencies are sensitive to load type and to classification accuracy even when resistive and elastic loads are not distinguishable subjectively.

Author (Hemer)

A95-75270

CONTINUOUS NEGATIVE AIRWAY PRESSURE INCREASES TONIC ACTIVITY IN DIAPHRAGM AND INTERCOSTAL MUSCLES IN HUMANS

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The main objective of the present study was to quantify the increase in tonic inspiratory activity (delta TIA) in response to continuous negative airway pressure (CNAP) in humans. TIA represents the activity in inspiratory muscles at the end of expiration. In 20 subjects, electromyograms (EMGs) were recorded from the diaphragm and parasternal intercostal muscles (ICM) with surface electrodes during control and at three different levels of CNAP. From these recordings we determined delta TIA and the amplitudes of phasic EMG activities (EMGphas) during CNAP and control. To evaluate the effects of CNAP on functional residual capacity (FRC), respiratory frequency, tidal volume, and minute ventilation, the subjects were connected to a closed breathing circuit. When the pressure at the airway opening was -0.9 kPa, mean values of delta TIA were 53 and 49% of control EMGphas for the diaphragm and ICM, respectively. In addition, EMGphas at airway opening pressure of -0.9 kPa had increased to 195 and 162% of control EMGphas for the diaphragm and ICM, respectively. The concomitant decrease in FRC was on average 18.7% of predicted FRC. Minute ventilation had increased significantly at all levels of CNAP compared with control. We conclude that CNAP is a forceful stimulus to increase TIA in humans in both the diaphragm and the ICM.

Author (Hemer)

A95-75271

PERMEABILITY OF FERRET TRACHEA IN VITRO TO (99M)-TC-DTPA AND (C-14)ANTIPYRINE

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Platelet-activating factor (PAF) and vasoactive drugs were tested on permeability of ferret trachea in vitro by measuring fluxes of (99m)-Tc-diethylenetriamine pentaacetic acid ((99m)-Tc-DTPA; hydrophilic) and (C-14)antipyrine ((C-14)AP; lipophilic) across the tracheal wall. Tracheae were bathed on both sides with Krebs-Henseleit buffer, with luminal buffer containing either (99m)-Tc-DTPA or (C-14)AP. Luminal and abluminal radioactivities, potential difference, and tracheal smooth muscle tone were measured. PAF (10 μ M) increased permeability to (99m)-Tc-DTPA, but permeability to (C-14)AP did not change, suggesting that paracellular but not transcellular transport was affected. Abluminal and luminal applications of methacholine, phenylephrine, and albuterol caused no change in permeability to (99m)-Tc-DTPA before or after exposure to luminal PAF, but abluminal histamine significantly increased permeability. Abluminal Hist decreased permeability to (C-14)AP before and after exposure to PAF. MCh, PE, and Hist increased smooth muscle tone; Alb and PAF had no effect. Thus, only PAF and Hist altered permeability to (99m)-Tc-DTPA, and MCh, PE, and Hist changed smooth muscle tone. Tracheal permeability changes were greater for the hydrophilic than for the lipophilic agent.

Author (revised by Hemer)

A95-75272

TGF-BETA(SUB 1) CAUSES INCREASED ENDOTHELIAL ICAM-1 EXPRESSION AND LUNG INJURY

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Neutrophil adherence to vascular endothelium is partially mediated by adhesion molecules, including intracellular adhesion molecule 1 (ICAM-1), on endothelial cells. We examined the effect of transforming growth factor-beta(sub 1) (TGF-beta(sub 1)) on the expression of ICAM-1 in human umbilical vein endothelial cells (HUVEC). TGF-beta(sub 1) (1 ng/ml) increased ICAM-1 and ICAM-1 mRNA expression in HUVEC, as assessed by flow cytometry and Northern blot analysis, respectively. In addition, we investigated whether exogenous recombinant TGF-beta(sub 1) can cause neutrophil-mediated lung injury in guinea pigs. The plasma half-life of I-125-labeled TGF-beta(sub 1) in guinea pigs was 4.6 \pm 0.1 min, and the I-125 activity was 2.8 \pm 0.2% 8 h after injection. The ratio of I-125-labeled albumin concentration in lung tissue and bronchoalveolar lavage (BAL) fluid to that in plasma, lung wet-to-dry weight ratio, numbers of neutrophils in BAL fluid, and numbers of neutrophils per alveolus in fixed lung sections increased in guinea pigs that received a high dose of TGF-beta(sub 1) compared with the control group. These results suggest that TGF-beta(sub 1) causes neutrophil-mediated lung injury, possibly through upregulation of ICAM-1 on endothelial cells, and might be important in the pathogenesis of lung injury.

Author (Hemer)

A95-75273

EFFECTS OF NO SYNTHASE INHIBITION ON THE MUSCULAR BLOOD FLOW RESPONSE TO TREADMILL EXERCISE IN RATS

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The functional role of nitric oxide (NO) release in regulating blood flow (BF) to exercising skeletal muscle was studied in conscious male Sprague-Dawley rats. In this study, BF was measured using radiolabeled microspheres during treadmill exercise (10% grade, 20 m/min) before and after NO synthase (NOS) inhibition with N(sup G)-nitro-L-arginine methyl ester (30 mg/kg ia). After NOS inhibition, mean arterial blood pressure increased from resting baseline values and the duration of vasodilator responses to acetylcholine (ACh) injections was diminished, demonstrating reduced NOS function. During exercise, BF to the kidneys and organs of the gut was reduced after NOS inhibition. In addition, BF was reduced in 16 of the 28 individual hindquarter muscles or muscle parts. Moreover these reductions in BF were linearly correlated with the estimated sum of the percentage of fast-twitch oxidative glycolytic (FOG) and slow-twitch oxidative (SO) types of fibers found in each muscle. These results suggest that NO-mediated vasodilation contributes to the BF responses within and among the muscles of the rat's hindquarters during exercise.

Author (Hemer)

A95-75274

REMOVAL OF ALBUMIN MICROINJECTED IN RAT LUNG PERIMICROVASCULAR SPACE

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We used a microinjection approach to assess hydraulic properties of lung perimicrovascular adventitia (interstitial cuff surrounding microvessels). Isolated blood-perfused rat lungs held at constant airway pressure were microscopically viewed to identify subpleural venules. Venular adventitia were microinjected with 20 nl of fluorescent albumin, and then adventitial fluorescence was quantified at the injection site by either photometry or imaging. Nonlinear decay of adventitial fluorescence indicated liquid flux from the injection site into normal interstitium. In some experiments, we determined that the adventitial fluorescence flowed longitudinally along the venule length and filled single lymphatics. The fluorescence decay at the injection site was best described by equations of convective but not diffusive transport. The decay time constant (time to 37% initial), which relates inversely to hydraulic conductivity, increased 10-fold above baseline on lung expansion with airway pressure from 5 to 15 cmH₂O. However, presence or absence of blood flow, increase in filtration pressure, and tissue edema were all without effect on the time constant. Our estimate of the lower limit of baseline adventitial hydraulic conductivity was 5 \times 10(exp -6) ml/sq cm/microvascular adventitia is not augmented by edema but that it is decreased by lung expansion.

Author (Hemer)

A95-75275

DOWNREGULATION OF PULMONARY ATRIAL NATRIURETIC PEPTIDE RECEPTORS IN RATS EXPOSED TO CHRONIC HYPOXIA

JAMES R. KLINGER, FRANK ARNAL, ROD R. WARBURTON, LO-CHANG OU, and NICHOLAS S. HILL *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1309-1316 (Contract(s)/Grant(s): NIH-HL-45050)

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We hypothesized that a downregulation in pulmonary atrial natriuretic peptide (ANP) receptors helps raise plasma ANP levels during chronic hypoxia. We measured in vivo pulmonary uptake and plasma clearance of I-125-ANP and in vitro pulmonary binding kinetics of I-125-ANP in normoxic and chronically hypoxic rats. Exposure to 21 days of hypobaric (0.5 atm) hypoxia did not decrease specific binding of I-125-ANP in the kidney, but pulmonary binding

decreased 35 and 75% after 1 and 3 days of hypoxia, respectively, and increased 200% after 3 days of normoxic recovery from 21 days of hypoxia. The total binding capacity for ANP to lung membrane fractions from normoxic rats, chronically hypoxic rats, and rats that had recovered from hypoxia was 488 ± 59 , 109 ± 17 , and 338 ± 48 fmol/mg, respectively. The area under the I-125-ANP plasma concentration curve for normoxic and hypoxic rats and normoxic rats that were infused with the ANP C-receptor ligand C-ANF-(4-23) was $3,292 \pm 216$, $5,022 \pm 466$, and $8,205 \pm 1,059$ disintegrations/min/ml, respectively. We conclude that pulmonary ANP clearance is reduced during chronic hypoxia secondary to a downregulation in pulmonary ANP clearance receptors. Reduced pulmonary clearance of ANP may represent an adaptation that contributes to increased plasma ANP levels during chronic hypoxia.

Author (Herner)

A95-75276

EFFECT OF LONG-TERM ELECTRICAL STIMULATION ON VASCULAR SUPPLY AND FATIGUE IN CHRONICALLY ISCHEMIC MUSCLES

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Fast skeletal muscles of Sprague-Dawley rats (tibialis anterior (TA) and extensor digitorum longus (EDL)) were subjected to ischemia by unilateral ligation of the common iliac artery. In some animals, ischemia was combined with indirect electrical stimulation at 10 Hz either for 3 x 2 h (strenuous activity) or for 7 x 10-min bouts/day (mild activity). After 2 wk, muscle blood flow and fatigue flow were measured during 5-min isometric supramaximal twitch contractions at 4 Hz. Terminal arteriole diameters were assessed in TA by intravital microscopy at rest and during contractions. Vascular perfusion in the muscles was estimated from measurements in the carotid and saphenous arteries below the site of ligation. Capillary supply was expressed in TA and EDL as capillary-to-fiber ratio on the basis of histochemical staining for capillaries. Strenuous stimulation of ischemic muscles increased their atrophy, failed to restore blood flow, and actually worsened fatigue. In contrast, mild stimulation improved perfusion pressure, increased capillary-to-fiber ratio in the glycolytic part of TA, restored dilatation of terminal arterioles during muscle contractions, and improved blood flow and muscle fatigue so that they were no longer significantly different from control muscles. Thus, an attenuated intermittent protocol may be indicated in the treatment of muscle ischemia.

Author (Herner)

A95-75277

EFFECTS OF ONO-5046, A SPECIFIC NEUTROPHIL ELASTASE INHIBITOR, ON ENDOTOXIN-INDUCED LUNG INJURY IN SHEEP

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The purpose of the present study was to assess the role of polymorphonuclear leukocyte (neutrophil) elastase in endotoxin-induced acute lung injury in sheep with lung lymph fistula. We studied the effects of ONO-5046, a specific inhibitor of neutrophil elastase, on the lung dysfunction induced by the intravenous infusion of 1 microgram/kg of *Escherichia coli* endotoxin. Endotoxin

alone produced a biphasic response as previously reported. Early (0.5 - 1 h) after endotoxin, pulmonary arterial pressure increased from 19.5 ± 0.9 cmH₂O at baseline to a peak of 46.8 ± 2.4 cmH₂O. Pulmonary vascular resistance increased from 3.03 ± 0.17 cmH₂O/l/min at baseline to a peak of 9.77 ± 0.70 cmH₂O/l/min. Circulating neutrophils decreased from $7,355 \pm 434$ cu mm at baseline to a nadir of $1,762 \pm 32$ cu mm. Thromboxane B₂ and 6-ketoprostaglandin F(sub 1 alpha) concentrations in plasma and lung lymph were significantly increased. Late (3 - 5 h) after endotoxin, pulmonary arterial pressure and pulmonary vascular resistance returned to baseline levels, but lung lymph flow remained increased from 4.2 ± 0.3 ml/0.5 h at baseline to 7.3 ± 0.7 ml/0.5 h, with a slight increase in lung lymph-to-phase protein concentration ratio, suggesting increased pulmonary vascular permeability. The histopathological features of the lungs during the early period in sheep treated with endotoxin alone revealed a large increase in neutrophils per 100 alveoli and changes of pulmonary edema such as thickening of the interstitium of the lung and alveolar flooding. The continuous intravenous infusion of ONO-5046 at 10 mg/kg/h blocked most of the lung dysfunction and histopathological changes of the lungs induced by endotoxin. We conclude that neutrophil elastase might have a crucial role in the pathogenesis of endotoxin-induced acute lung injury in sheep.

Author (Herner)

A95-75278

EFFECT OF HEMATOCRIT ON SYSTEMIC O₂ TRANSPORT IN HYPOXIC AND NORMOXIC EXERCISE IN RATS

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The effect of hematocrit (Hct) on O₂ transport in hypoxic (inspired PO₂ (P_I(sub O₂)) approximately 70 Torr) and normoxic (P_I(sub O₂)) approximately 145 Torr) exercise was studied in rats acclimatized to 3 wk of P_I(sub O₂) at approximately 70 Torr (A rats) and in nonacclimatized littermates (NA rats). Isovolumic exchange transfusion of plasma or red blood cells was used to lower Hct in A rats from approximately 60 to 45% and to raise Hct of NA rats from 45 to 60%. Controls were A and NA rats exchange transfused with whole blood at constant Hct. Lowering Hct of A rats lowered the arterial O₂ concentration (Ca(sub O₂)) and the arterial-mixed venous O₂ difference and increased the maximal cardiac output (dot-Q MAX) without changes in maximal O₂ uptake (dot-VO₂(sub MAX)) or in the product of dot-Q MAX x Ca(sub O₂), circulatory O₂ convection at maximal exercise (dot-TO₂(sub MAX)). Raising Hct in NA rats produced the opposite changes in Ca(sub O₂), arterial-mixed venous O₂ difference, and dot-Q MAX, but dot-VO₂(sub MAX) and dot-TO₂(sub MAX) increased significantly, both in hypoxia and normoxia, because of relatively small changes in dot-Q MAX. In NA rats, a steeper slope of the line relating dot-VO₂(sub MAX) to calculated mean capillary PO₂ at high Hct suggested a higher tissue O₂ diffusing capacity with high Hct. For a given Hct and dot-Q MAX, systemic arterial pressure was higher in A rats. The data suggest that (1) the effect of Hct on systemic hemodynamics is different in A and NA rats, resulting in different effects dot-VO₂(sub MAX); (2) factors in addition to Hct contribute to the high systemic vascular resistance of A rats; and (3) increased diffusive conductance for O₂, as well as increased dot-TO₂(sub MAX), could be responsible for the effect of Hct on dot-VO₂(sub MAX) of NA rats.

Author (Herner)

A95-75279

VENTILATOR PATTERN INFLUENCES NEUTROPHIL INFLUX AND ACTIVATION IN ATELECTASIS-PRONE RABBIT LUNG

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Both ventilator pattern and neutrophil activation influence lung injury in adult respiratory distress syndrome (ARDS). We therefore questioned whether ventilator pattern independently affects neutrophil accumulation and function in early ARDS. Thirty-five New Zealand White rabbits were anesthetized, paralyzed, and prepared using sterile techniques. Fifteen surfactant-depleted animals were randomized and ventilated for 4 h using high-frequency oscillatory ventilation (HFO) at 15 Hz with an inspired O₂ fraction = 1.0 and arterial PO₂ (Pa(sub O₂)) greater than 400 Torr (a pattern known to reverse atelectasis) or conventional mechanical ventilation (CMV) with Pa(sub O₂) = 80 - 100 Torr (a pattern with some atelectasis despite positive end-expiratory pressure). Eight normal animals on CMV with Pa(sub O₂) greater than 400 Torr served as a reference group (NorCMV). NorCMV animals progressively increased circulating polymorphonuclear neutrophil (PMN) numbers and had minor pressure-volume curve alterations but no other significant changes. Lavaged CMV animals developed the characteristic gas exchange and marked pressure-volume curve abnormalities of ARDS. Circulating PMNs remained constant but developed decreased chemotactic activity, whereas lung neutrophil numbers increased significantly ($P = 0.0002$) and had substantially enhanced chemiluminescence ($P = 0.0003$ vs. NorCMV animals). Although lavaged HFO animals accumulated an intermediate number of lung neutrophils (lung myeloperoxidase greater than NorCMV animals; $P = 0.0003$), the chemiluminescence and chemotaxis of these PMNs were the same as in cells from NorCMV animals. We concluded that both the degree of neutrophil activation and lung injury can be minimized by preventing cyclic alveolar/airway expansion and collapse in the surfactant-deficient lung by use of appropriate ventilator patterns.

Author (Hemer)

A95-75280**ENDURANCE EXERCISE TRAINING IS ASSOCIATED WITH ELEVATED BASAL SYMPATHETIC NERVE ACTIVITY IN HEALTHY OLDER HUMANS**

ALEXANDER V. NG, ROBIN CALLISTER, DAVID G. JOHNSON, and DOUGLAS R. SEALS Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1366-1374 (Contract(s)/Grant(s): NIH-AG-06537; NIH-HL-39966; NIH-AG-05518; NIH-AG-00423)

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We tested the hypothesis that endurance training is associated with altered basal levels of muscle sympathetic nerve activity (MSNA) and responses to acute stress in healthy older adults. MSNA (peroneal microneurography) and plasma norepinephrine (NE) concentrations were measured during supine rest, a cold pressor test, and isometric handgrip (40% maximal voluntary force to exhaustion) in 16 older masters endurance athletes and 15 healthy normotensive untrained control subjects. The athletes had higher levels of estimated daily energy expenditure and maximal oxygen uptake and lower levels of resting heart rate and body fat than the control subjects. MSNA during supine rest was elevated in the athletes whether expressed as burst frequency or burst incidence. These whole group differences were due primarily to markedly higher levels of MSNA in the athletic vs. untrained women. In contrast, basal plasma NE concentrations were not significantly different in the athletes vs. control subjects. The MSNA and plasma NE responses to acute stress tended to be greater in the athletes. These findings indicate that vigorous regular aerobic exercise is associated with an elevated level of MSNA at rest and a tendency for an enhanced response to acute stress in healthy normotensive older humans.

Author (revised by Hemer)

A95-75281**GRAVITATIONAL AND SHEAR-ASSOCIATED PRESSURE GRADIENTS IN THE ABDOMEN**

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of Public Health, Boston, MA, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1375-1382 (Contract(s)/Grant(s): NIH-HL-33009) (HTN-95-A0712) Copyright

The abdomen has been variously characterized as a hydrostatic system, in which pressures exhibit a gravitational gradient and pressure fluctuations are spatially uniform, and as a compartment, in which pressure gradients are not simply gravitational and pressure fluctuations differ markedly from place to place. To characterize the pressures acting on the ventral abdominal wall, we used saline-filled catheters and air-filled balloons in anesthetized dogs in various body positions during spontaneous breathing and mechanical ventilation. Pressures were measured in the stomach and at multiple sites next to the abdominal wall. Under most circumstances, measurements next to the abdominal wall exhibited a hydrostatic gravitational gradient of approximately 0.89 cmH₂O/cm height and pressure fluctuations were spatially homogeneous. Deviations from this hydrostatic behavior were seen when abdominal pressures were compared with gastric pressures, when measurements were made with a balloon catheter, and when the lower abdomen was constricted with a binder. Analysis of these and previously published data suggests that the abdomen does, at times, behave like a hydraulic system but can deviate from simple hydrostatic behavior to the extent that shape-stable abdominal viscera are deformed.

Author (Hemer)

A95-75282**AN APPROACH TO THE STUDY OF UPPER AIRWAY FUNCTION IN HUMANS**

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Current methods for testing upper airway (UA) collapsibility in humans tend to produce intervention-related changes in some of the variables that affect UA stability. Therefore, their results may not reflect UA stability under the experimental conditions of interest. In the proposed method, the subject lies in a body enclosure with head and neck out. Pressure is altered in brief pulses to avoid behavioral responses. The collapsibility of UA under 'static' conditions is tested by delivering identical pressure pulses simultaneously to the airway and body surface inside the shell. Because the pressure applied to the respiratory system is not altered, cessation of flow indicates closure, and the pressure at which this happens is P_{closure}. Collapsibility under dynamic conditions is tested by applying brief negative pulses to the shell only, thereby forcing an increase in inspiratory flow. Ten normal awake subjects were tested. None of the subjects developed closure when negative pulses were applied to both airway and shell during inspiration or expiration with either nose or mouth breathing. There were only small reductions in flow, indicating minor narrowing. By contrast, pressure pulses of similar magnitude applied to the shell alone were associated with closure in 5 of 10 subjects. We conclude that the UA of normal awake humans is fairly stable under the influence of statically applied pressure but susceptible to collapse under conditions of increased flow. P_{closure} determined under static conditions underestimates the vulnerability of the UA to collapse under dynamic conditions. Author (Hemer)

A95-75283**ABDOMINAL MUSCLE ACTIVITY DURING HYPERCAPNIA IN AWAKE DOGS**

A. M. LEEVERS British Columbia Univ., Vancouver, Canada and J. D. ROAD British Columbia Univ., Vancouver, Canada Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1393-1398 Research sponsored by Medical Research Council of Canada (HTN-95-A0714) Copyright

We previously found the internal abdominal muscle layer to be preferentially recruited during expiratory threshold loading in anesthetized and awake dogs. Expiratory threshold loading increases end-expiratory lung volume and hence can activate reflex pathways such as tonic vagal reflexes, which could influence abdominal muscle recruitment. Our objectives in the present study were to determine the effects of hypercapnia on abdominal muscle activation and the pattern of recruitment in awake dogs. Five tracheotomized dogs were chronically implanted with sonomicrometer transducers and fine-wire electromyogram (EMG) electrodes in each of the four abdominal muscles: transversus abdominis, internal oblique, external oblique, and rectus abdominis. Muscle length changes and EMG activity were studied in the awake dog at rest and during CO₂ rebreathing. CO₂ rebreathing produced a tripling of tidal volume and activation of the abdominal muscles. Despite the increase in tidal volume, there was no significant change in abdominal muscle end-inspiratory length. Both tonic and phase expiratory shortening were greater in the internal muscle layer (transversus abdominis and internal oblique) than in the external muscle layer (external oblique and rectus abdominis). We conclude that the internal abdominal muscles are preferentially recruited by hypercapnia and vagal reflexes probably do not contribute to this differential recruitment but that segmental reflexes may be involved. The mechanical consequences of this recruitment are discussed. Author (Hemer)

A95-75284

ALTERATION OF PLASMA ENDOTHELIN-1 BY EXERCISE AT INTENSITIES LOWER AND HIGHER THAN VENTILATORY THRESHOLD

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The purpose of this study was to investigate whether the release of endothelin-1 (ET-1), a potent vasoconstrictor peptide produced by vascular endothelial cells, is induced by exercise. Venous plasma concentrations of ET-1 were measured by sandwich-enzyme immunoassay before and after endurance exercise with a cycle ergometer at different intensities. Male intercollegiate athletes participated in the study and performed cycle ergometer exercise of 30 min duration at intensities of 90 or 130% of their individual ventilatory threshold (VT). The plasma concentration of ET-1 was slightly but significantly increased after exercise at 90% and markedly increased after exercise at 130% of individual VT. The increase in ET-1 was greatest 30 min after exercise at both intensities. It was first demonstrated that the plasma concentration of ET-1 was significantly increased after exercise: the greater the intensity, the greater the extent of the increase in plasma ET-1 concentration. However, the precise physiological roles of ET-1 during exercise remain to be elucidated. Author (Hemer)

A95-75285

ARM MUSCLE SYMPATHETIC NERVE ACTIVITY DURING PREPARATION FOR AND INITIATION OF LEG-CYCLING EXERCISE IN HUMANS

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We tested the hypothesis that sympathetic vasoconstrictor nerve activity to nonactive skeletal muscle (MSNA) decreases immediately before and remains suppressed during initiation of conventional large muscle upright dynamic exercise in humans. In 11 healthy young subjects, adequate recordings of MSNA from the radial nerve in the arm were obtained during upright seated rest

(control) and throughout 1 min of leg-cycling exercise at one or more submaximal workloads. MSNA was analyzed during four consecutive time intervals: control, preparation for cycling (end of control to onset of pedal movement), initiation of cycling (onset of pedal movement to attainment of target power output), and the initial 60 s of cycling at target power output. MSNA decreased abruptly and markedly in all subjects during the preparation period before the 33-W load and remained suppressed throughout the period of initiation of cycling in 8 of 11 subjects; MSNA increased during the initiation period in three subjects in whom diastolic arterial pressure fell below control levels. This general pattern was observed at all loads. MSNA remained at or below control levels throughout the 1 min of cycling exercise at 33 - 166 W. MSNA increased above control levels during the latter portion of the 1 min of cycling only at loads equal to or greater than 60% of peak power output. Our results indicate that MSNA in a relaxed arm is almost completely inhibited during a period of preparation for leg-cycling exercise, remains suppressed during the initiation of exercise in most subjects, and increases above control levels only during the initial minute of cycling at moderate-to-heavy submaximal exercise intensities. Author (Hemer)

A95-75286

EFFECTS OF SPACEFLIGHT ON MORPHOLOGY OF THE RAT ADENOHYPOPHYSIS

KAMAL THAPAR, KALMAN KOVACS, EVA HORVATH, LUCIA STEFANEANU, EIZABETH CHAMBERS, and ALAN J. MORTIMER Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1141-1420 Research sponsored by Canadian Space Agency, Physicians Services Inc. Foundation of Ontario, and Toronto Univ.

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To determine the effects of spaceflight on the anterior pituitary gland, the adenohypophyses of rats after a 7-day spaceflight aboard the space shuttle Endeavor (STS-54) were investigated by histology, immunohistochemistry, morphometry, electron microscopy, and in situ hybridization and were compared with synchronous control rats. Morphometry revealed the corticotrophs of space-flown rats to be significantly enlarged, demonstrating 46 - 48% increases in mean cell, nuclear, and cytoplasmic areas. These corticotrophs also exhibited striking ultrastructural signs of heightened secretory activity. Furthermore, their expression of proopiomelanocortin mRNA, the transcript encoding the precursor protein from which adrenocorticotrophic hormone is posttranslationally cleaved, was also significantly enhanced, a finding consistent with their hypersecretory state. Gonadotrophs also exhibited significant increments in mean nuclear, cell, and cytoplasmic areas of 22, 45, and 51%, respectively; however, they were not accompanied by ultrastructural evidence of increased secretory function. There were no morphological changes in somatotrophs, lactotrophs, or thyrotrophs, nor were there any significant changes in the overall frequency of any one adenohypophyseal cell type in comparison with control. The structural integrity of all adenohypophyseal secretory and vascular elements was preserved after spaceflight, as there was neither evidence of necrosis nor other forms of cellular injury in spaceflown specimens. Capillaries were patent, and neither endothelial damage nor thrombosis was noted. These data suggest that spaceflight is accompanied by a selective morphological response in the anterior pituitary, one characterized by hypertrophy of both corticotrophs and gonadotrophs and by enhanced endocrine activity of the former. Author (Hemer)

A95-75287

ECCENTRIC CONTRACTION-INDUCED INJURY IN NORMAL AND HINDLIMB-SUSPENDED MOUSE SOLEUS AND EDL MUSCLES

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The primary objective of this study was to compare the magni-

tude of injury in mouse extensor digitorum longus (EDL) and soleus muscles induced by high-force eccentric contractions. A second objective was to study the effect of altering the daily loading of the muscles through hindlimb suspension (HS) on the injury. One of two protocols was performed in vitro: (1) 15 eccentric contractions or (2) 15 isometric contractions. Immediately after the eccentric contraction protocol, markedly greater decrements in maximal isometric tetanic force ($P(\text{sub } o)$) occurred in the normal EDL than in the normal soleus muscles. LDH release immediately after the eccentric contraction protocol was 2.7-fold greater in the normal EDL than in the normal soleus muscles. To investigate the role of recent loading of the muscles in the injury, EDL ($n = 9$) and soleus ($n = 10$) muscles from mice subjected to HS for 14 days performed the eccentric contraction protocol. HS resulted in greater decrements in contractile performance for the soleus muscles but not for the EDL muscles. HS resulted in a 76% greater LDH release in the soleus muscle but had no effect on LDH release by the EDL muscle. HS did not alter the histochemically determined fiber type composition of the soleus muscle. The data demonstrate that EDL muscles are more susceptible than soleus muscles to eccentric contraction-induced injury in normal weight-bearing mice; part of the explanation for the difference appears to be the greater previous loading of the soleus muscle rather than the fiber type composition per se.

Author (revised by Herner)

A95-75288

EFFECT OF INCREASING WORK RATE ON METABOLIC RESPONSES OF THE DONKEY (*EQUUS ASINUS*)

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Oxygen consumption dot-VO₂ and concentration of venous blood metabolites were measured in donkeys trained to run and to pull loads on a treadmill. Dot-VO₂ in two donkeys running at maximal speed on a 9.8% slope was 110 ± 2 ml/min/kg, approximately 22 times preexercise dot-VO₂. Average heart rate at maximal dot-VO₂ (dot-VO₂(sub MAX)) was 223 ± 2 beats/min, five times the preexercise heart rate. Blood lactate increased 14-fold and blood glucose did not change (P greater than 0.05). Animals running up a 4% incline and incremental draft loading of five donkeys walking on the level were also studied. The total energy cost of walking unloaded was 2.86 ± 0.06 J/m/kg live/wt. During low- to medium-intensity draft work for 25 min, glucose fell below preexercise values, whereas plasma hematocrit and cortisol increased. Blood lactate remained unchanged up to approximately 40% dot-VO₂(sub MAX) but increased 170% at approximately 60% dot-VO₂(sub MAX). The responses in donkeys are similar to those of exercising horses except for the rapid decline in blood glucose observed during low-intensity exercise and the lower lactate levels at both the high-intensity exercise and the apparent anaerobic threshold.

Author (Herner)

A95-75289

DECLINE RUNNING PRODUCES MORE SARCOMERES IN RAT VASTUS INTERMEDIUS MUSCLE FIBERS THAN DOES INCLINE RUNNING

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Unaccustomed eccentric exercise, in which a muscle is lengthened while generating tension, is well known to cause injury and pain. A rapid training effect has been demonstrated in a number of eccentric exercises. The mechanism for both the damage and the training has been unknown. Morgan proposed that the damage is

caused by sarcomere length instabilities during operation on the descending limb of the sarcomere length-tension curve and that the training effect is an increase in the number of sarcomeres connected in series in a muscle fiber, thus avoiding the descending limb. We tested this proposal by exercising rats on a treadmill set at either an incline or a decline of 16 deg, an exercise that has previously been shown to cause damage in untrained rats and a training effect. The vastus intermedius muscles were fixed and were digested in acid, and the fiber and sarcomere lengths of representative fibers were measured. From these measurements, the mean number of sarcomeres per fiber was found for the different training regimes. A clear and repeatable difference was found, supporting Morgan's prediction of more sarcomeres after decline running, although with some differences in response that depended on the age of the rats.

Author (Herner)

A95-75290

ENHANCED ENDOTHELIN-1 AND ENDOTHELIN RECEPTOR GENE EXPRESSION IN CHRONIC HYPOXIA

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To test the hypothesis that endothelin (ET)-1 synthesis and ET receptor levels are increased selectively in the lung of rats with chronic hypoxic pulmonary hypertension, the current study examined the effects of exposure to chronic hypoxia (10% O₂, 1 atm, 4 wk) on pulmonary arterial pressure, ET-1 levels in plasma and lung, and ET-1 and ET(sub A) and ET(sub B) receptor mRNA levels in lung, heart, pulmonary artery, aorta, kidney, spleen, and liver. Hypoxic exposure was associated with increases in pulmonary arterial pressure, plasma ET-1 levels, ET-1 mRNA in lung and pulmonary artery, and ET-1 stores and ET(sub A) and ET(sub B) receptor mRNA levels in lung. In thoracic aorta and the four heart chambers, ET(sub A) and ET(sub B) receptor mRNA levels were increased, but ET-1 mRNA levels were unchanged from air control levels. No change in ET-1 or ET receptor mRNA levels was seen in organs perfused by the systemic vascular bed, except in liver, where ET(sub A) receptor mRNA levels were decreased. The findings of concomitant increases in gene transcript levels for ET-1 and the ET(sub A) and ET(sub B) receptors in lung, but not in the great vessels or any other organ examined, are consistent with the hypothesis that increased ET-1 synthesis in the lung contributes to pulmonary vascular remodeling and the maintenance of chronic hypoxic pulmonary hypertension.

Author (Herner)

A95-75291

REDUCTION AND UPTAKE OF METHYLENE BLUE FROM RAT AIR SPACES

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The use of methylene blue (MB) to estimate dilution of epithelial lining fluid, which occurs during bronchoalveolar lavage (BAL) is complicated by loss of this redox dye from the air spaces. The rate of MB uptake from the air spaces of isolated rat lungs and the effects of oxidation and reduction on this process were investigated in this

study. Movement of MB from the air spaces to perfusate was compared with the corresponding transport of I-125-labeled albumin, (c-14)-dextran, (99 m)TC labeled diethylenetriamine-pentaacetate, (H-3)-sucrose, and (3)H₂O. By the end of 2 min, MB concentrations in the BAL had fallen by 58 \pm 4% (SE; n = 11) and (3)H₂O by 78 \pm decreased by approximately 6%. All but 10% of the (3)H₂O lost from the air spaces was found in the perfusate, whereas 19% of the lost MB was not recovered in the perfusate, suggesting retention of MB in the pulmonary tissues. Absorption of MB from the air spaces was slowed by 20% when the lungs were left unperfused, and absorption was accelerated threefold by reduction of MB to leukomethylene blue with Na₂S₂O₄. In contrast, MB losses from the air space were slowed by the oxidizing agent K₃Fe(CN)₆ and by addition of superoxide dismutase or ascorbic oxidase. It is therefore possible that ascorbic acid and O₂(-) entering the air spaces reduce MB to the uncharged leuko form. Lowering the pH of the BAL fluid to 3.5 also slowed MB reabsorption. This suggests that acid aspiration may stimulate release of oxidants into the air spaces.

Author (Hemer)

A95-75292

THROMBOXANE A(SUB 2) MIMETIC U-46619 INDUCES SYSTEMIC AND PULMONARY HYPERTENSION AND DELAYED TACHYPNEA IN THE GOAT

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Cardiorespiratory variables were measured continuously in five conscious goats before and after the infusion of U-46619 at a dose of either 2, 4, or 6 micrograms/kg/5 min. Infusion of U-46619 led to immediate increases in pulmonary arterial blood pressure (ABP) that were sustained for up to 15 min after the end of the infusion. Systemic ABP also increased, but the relative increase from control was less than the pulmonary pressor response. At the highest dose, U-46619 elicited a delayed tachypneic response that was greatest several minutes after the infusion was stopped. U-46619 was also infused simultaneously with sodium nitroprusside to clamp ABP pressure at baseline levels to determine whether stimulation of baroreceptors might contribute to the latency of the tachypneic response. Although sodium nitroprusside infusion prevented the increase in ABP, the increase in breathing frequency was still delayed 3 - 4 min from the start of the infusion. We conclude that U-46619 elicits pulmonary and systemic arterial hypertension in the conscious goat. At the higher dose U-46619 also elicits a delayed tachypnea that remains delayed even if ABP is normal.

Author (Hemer)

A95-75293

EFFECTS OF PULMONARY BLOOD FLOW ON THE FRACTAL NATURE OF FLOW HETEROGENEITY IN SHEEP LUNGS

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The spatial heterogeneity of pulmonary blood flow can be described by the relative dispersion (RD) of weight-flow histograms ($RD = SD/mean$). Glenny and Robertson (1990) showed that RD of flow in the lung is fractal in nature, characterized by the fractal dimension (D) and RD for the smallest realizable volume element (RD sub ref). We studied the effects of increasing total pulmonary blood flow on D and RD(sub ref). In eight in situ perfused sheep lung preparations, 15-micrometer radio-labeled microspheres were injected into the pulmonary artery at five different blood flows ranging, in random order, from 1.5 to 5.0 l/m. The lungs were in zone 2 at the

lower flows and in zone 3 at the higher flows. The lungs were removed, dried, cut into 2 x 2 x 2-cu cm pieces, weighed, and then counted for microsphere radioactivity. Fractal plots of log (weight) vs. log (RD) were constructed by iteratively combining neighboring pieces and then calculating RD with the increasingly larger portion size. D, which is one minus the slope of the fit through this plot, was 1.14 \pm 0.09 and did not change as blood flow increased. However, RD(sub ref) decreased significantly as total flow increased. We conclude that the fractal nature of pulmonary blood flow distribution is not altered by changes in overall flow.

Author (Hemer)

A95-75294

REDUCTION AND ACCUMULATION OF METHYLENE BLUE BY THE LUNG

ROBERT D. BONGARD, GARY S. KRENZ, JOHN H. LINEHAN, DAVID L. ROERIG, MARILYN P. MERKER, JEFFREY L. WIDELL, and CHRISTOPHER A. DAWSON *Journal of Applied Physiology* (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1480-1491 Research sponsored by Dept. of Veterans Affairs (Contract(s)/Grant(s): NIH-HL-24349) (HTN-95-A0725) Copyright

We studied the disposition of methylene blue added to the perfusate passing through isolated perfused rabbit lungs. Experiments were carried out in a recirculating or single-pass mode, the latter with either a steady infusion or bolus injection of the dye in its blue oxidized form (MB(+)) or in its colorless reduced leukomethylene blue form (MBH). The recirculation experiments revealed that the dye was taken up by the lungs and that a substantial fraction (approximately 16% of the MB(+)) entering the pulmonary artery was reduced before it emerged from the pulmonary veins. Sequestration of the dye by the lungs was a relatively slow process, and the blue color of the lungs at a time when there was little dye left in the perfusate suggests that much of the sequestered dye was in the oxidized form. The results from the single-pass bolus and steady infusion experiments suggest that MBH diffuses rapidly between perfusate and tissue and that it is more soluble in the tissue than in the perfusates used in the study. In this context, the concept of 'solubility' includes the impact of the rapidly equilibrating associations of the dye with the perfusate albumin and tissue components. The observed characteristics of the disposition of the methylene blue within the lungs and the rapid rate of its reduction on passage through the lungs suggest that it may be useful to evaluate the possibility that changes in reduction, uptake, and/or sequestration rates may reflect alterations in the metabolic function of the lungs.

Author (Hemer)

A95-75295

OZONE-INDUCED LOSS OF NEURONAL M(SUB 2) MUSCARINIC RECEPTOR FUNCTION IS PREVENTED BY CYCLOPHOSPHAMIDE

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We tested the hypothesis that inflammatory cells mediate the loss of neuronal M(sub 2) muscarinic receptors in the lung after ozone exposure. Pathogen-free guinea pigs treated with cyclophosphamide before exposure to ozone were compared with untreated ozone-exposed animals. This dose of cyclophosphamide significantly reduced leukocytes in peripheral blood and bronchoalveolar lavage fluid. Twenty-four hours after ozone, muscarinic receptor function was tested in anesthetized animals. In air-exposed guinea pigs, vagally induced bronchoconstriction was attenuated by the muscarinic agonist pilocarpine and potentiated by the selective M(sub 2) antagonist gallamine, indicating that the neuronal M(sub 2) muscarinic receptors were functioning. These responses were significantly reduced after ozone, indicating loss of neuronal M(sub 2)

muscarinic receptor function. However, in those animals treated with cyclophosphamide, M(sub 2) muscarinic receptor function was not altered by ozone. These data suggest that ozone-induced loss of neuronal muscarinic receptor function is mediated via inflammatory cells and that the link between ozone-induced hyperresponsiveness and inflammation may be the neuronal M(sub 2) muscarinic receptor.

Author (Herner)

A95-75296

CARDIOVASCULAR RESPONSES TO EXHAUSTIVE UPRIGHT CYCLE EXERCISE IN HIGHLY TRAINED OLDER MEN

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It is unclear whether the markedly enhanced aerobic exercise capacity of older endurance-trained men relative to their sedentary age peers is mediated primarily by central or peripheral cardiovascular mechanisms. To address this question, we performed radionuclide ventriculography with respiratory gas exchange measurements during exhaustive upright cycle ergometry in 16 endurance-trained men aged 63 \pm 7 yr and in 35 untrained men of similar age. As expected, maximal O₂ consumption during treadmill exercise was much higher in athletes than in controls. At rest and during fixed submaximal cycle work rates through 100 W, athletes demonstrated lower heart rates and greater stroke volume indexes than controls while maintaining similar cardiac indexes and O₂ uptake (dot-VO₂). At exhaustion, athletes achieved 53% higher work rates and peak dot-VO₂ per kilogram body weight than the sedentary men. The higher peak dot-VO₂ in athletes was achieved by a 22.5% larger cardiac index and a 15.6% greater arteriovenous O₂ difference. The larger peak cardiac index in the athletes than in sedentary controls was mediated entirely by a greater stroke volume index; peak heart rates were virtually identical. The athletes' greater stroke volume index was achieved through an 11% larger end-diastolic volume index and a 7% higher ejection fraction, both of borderline significance. At exhaustion, athletes demonstrated a lower systemic vascular resistance than controls, despite a higher value at rest. Athletes also showed greater exercise-induced increments in heart rate, stroke volume index, and cardiac index and a greater reduction in systemic vascular resistance from rest to maximal workload. Thus the higher aerobic capacity in endurance-trained older men during exhaustive upright cycle ergometry than in their sedentary age peers is achieved through central and peripheral mechanisms, which are of similar magnitude.

Author (Herner)

A95-75297

PERIPHERAL VASOCONSTRICTION SHORTLY AFTER ONSET OF MODERATE EXERCISE IN HUMANS

KARIN TOSKA Oslo Univ., Oslo, Norway and MORTEN ERIKSEN Oslo Univ., Oslo, Norway Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1519-1525
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The immediate cardiovascular responses at the onset of supine dynamic leg exercise were studied by noninvasive methods in healthy humans. Total peripheral conductance (TPC), heart rate, and cardiac output increased very rapidly at the onset of exercise. Mean arterial pressure (AMP) showed a moderate anticipatory increase during a 10-s countdown to exercise and then decreased (but not below resting level) during the first 10 s of exercise. The TPC response was biphasic, and TPC started to fall from its peak value approximately 12 s after onset of exercise. This peripheral vasoconstriction increased MAP. After 25 s, the cardiovascular variables were stable for the rest of the 2-min exercise period. In the same subjects, cholinergic blockade was

induced by atropine sulfate (0.035 mg/kg) and resting cardiac output, MAP, and TPC increased considerably. The exercise protocol was repeated after atropine, and the increase in heart rate at onset of exercise was slower and smaller. MAP decreased and remained depressed throughout the exercise period. A monophasic increase in TPC was seen. We suggest that, in the normal situation, the biphasic response in TPC reflects a baroreflex sympathetic vasoconstriction very shortly after onset of exercise and that this response is due to a rapid increase in set point for arterial pressure control at the onset of exercise. After cholinergic blockade, MAP was probably continuously well above the set point for arterial pressure control both before and during exercise and no reflex vasoconstriction was observed in this situation.

Author (Herner)

A95-75298

PHYSIOLOGICAL DEAD SPACE INCREASES DURING INITIAL HOURS OF CHRONIC HYPOXEMIA WITH OR WITHOUT HYPOCAPNIA

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A whole body plethysmograph was used to determine the minute ventilation-to-CO₂ production ratio (dot-VE/dot-VCO₂) of intact unrestrained unanesthetized adult male Sprague-Dawley rats during 7 days of hypoxemia (arterial PO₂ approximately 50 Torr). In one set of rats, normocapnia (arterial PCO₂ approximately 40 Torr) was maintained. Arterial blood gases and acid-base status were determined, and arterial PCO₂ was used to calculate alveolar ventilation-to-dot-VCO₂ ratio (dot-VA/dot-VCO₂) in all situations when inhaled CO₂ was not elevated. In normoxia dot-VE/VCO₂ = 25 \pm 1 (mean \pm 95% confidence limits); after 12 h of hypoxemia, dot-VE/dot-VCO₂ was maximal, 61 \pm 5 in hypoxemic hypocapnia and 200 \pm 55 in hypoxemic normocapnia. Between 2 and 7 days of hypoxemia, dot-VE/dot-VCO₂ had plateaued, 42 \pm 3 in hypoxemic hypocapnia and 95 \pm 19 in hypoxemic normocapnia. Dead space-to-tidal volume ratio (VD/VT) = (dot-VE/dot-VCO₂ - dot-VA/dot-VCO₂)/(dot-VE/dot-VCO₂), and in normoxia VD/VT = 0.17 \pm 0.04. In hypoxemic hypocapnia, VD/VT measured between 1 and 5 h was 0.38 \pm 0.04. It remained elevated at 0.29 \pm 0.04 after 24 h, but after 4 - 7 days in hypoxemic hypocapnia, VD/VT had recovered to 0.15 \pm 0.03. It is postulated that the disproportionate increase in dot-VE/dot-VCO₂ observed during the first 24 h of exposure to hypoxemic normocapnia (compared with elevated steady-state plateau levels maintained from 2 to 7 days sojourn) reflects an immediate transient increase of physiological dead space on exposure to hypoxemia.

Author (Herner)

A95-75299

EFFECT OF DETRAINING ON GLUT-4 PROTEIN IN HUMAN SKELETAL MUSCLE

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The present study was undertaken to examine the effect of 10 days of detraining on levels of GLUT-4 protein expression and citrate synthase (CS) activity in the vastus lateralis of trained men. During the course of normal training, seven endurance-trained (T) men and eight age- and weight-matched active but untrained (UT) men underwent an oral glucose tolerance test (OGTT) after an overnight fast. Muscle samples were obtained from the vastus lateralis by needle biopsy for measurement of GLUT-4 protein and CS activity. The tests were repeated on six of the T subjects after 10 days of detraining (DT men). The area under the insulin response curve during OGTT was lower in T men than in DT and UT men. There were

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no differences between groups in the glucose responses to OGTT. GLUT-4 protein levels and CS activity were higher in T men than in DT and UT men. Muscle GLUT-4 protein content was correlated with CS activity in all three groups ($r = 0.64, 0.68$, and 0.96 for UT, T, and DT men, respectively). These results suggest that muscle GLUT-4 protein content and oxidative capacity undergo parallel adaptations after detraining in previously well-trained men.

Author (revised by Herner)

A95-75300

EFFECT OF CARBOHYDRATE INGESTION ON GLUCOSE KINETICS DURING EXERCISE

GLENN MCCONELL Royal Melbourne Hospital, Melbourne Univ., Parkville, Australia, SUZANNE FABRIS Royal Melbourne Hospital, Melbourne Univ., Parkville, Australia, JOSEPH PROIETTO Royal Melbourne Hospital, Melbourne Univ., Parkville, Australia, and MARK HARGREAVES Royal Melbourne Hospital, Melbourne Univ., Parkville, Australia Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1537-1541 Research sponsored by National Health and Medical Research Council of Australia and Ross Australia (HTN-95-A0731) Copyright

Six well-trained men were studied during 2 h of exercise at 69 \pm 1% peak pulmonary oxygen uptake to examine the effect of carbohydrate (CHO) ingestion on glucose kinetics. Subjects ingested 250 ml of either a 10% glucose solution containing 6-(H-3) glucose (CHO) or a sweet placebo every 15 min during exercise. Glucose kinetics were assessed by 6,6-(H-2) glucose infusion corrected for gut-derived glucose in CHO. Plasma glucose was higher in CHO from 20 min. Total glucose appearance was higher in CHO due to glucose delivery from the gut, since hepatic glucose production was reduced by 51%. Glucose uptake was higher in CHO with the ingested glucose supplying 67 \pm 4 g and, with the assumption that it was fully oxidized, accounted for 14 \pm 1% of total energy expenditure. In conclusion, CHO ingestion during prolonged exercise results in suppression of hepatic glucose production and increased glucose uptake. These effects appear to be mediated mainly by increased plasma glucose and insulin levels.

Author (Herner)

A95-75301

PRIOR EXERCISE SUPPRESSES THE PLASMA TUMOR NECROSIS FACTOR RESPONSE TO BACTERIAL LIPOPOLYSACCHARIDE

GREGORY J. BAGBY Louisiana State Univ. Medical Center, New Orleans, LA, US, DAVID E. SAWAYA Louisiana State Univ. Medical Center, New Orleans, LA, US, LARRY D. CROUCH Louisiana State Univ. Medical Center, New Orleans, LA, US, and RAYMOND E. SHEPHERD Louisiana State Univ. Medical Center, New Orleans, LA, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1542-1547 Research sponsored by American Heart Association (Contract(s)/Grant(s): NIH-GM-32654) (HTN-95-A0732) Copyright

This study was initiated to determine the effect of physical exercise on the in vivo tumor necrosis factor- α (TNF) response to *Escherichia coli* lipopolysaccharide (LPS). Rats familiarized with treadmill running and surgically implanted with vascular catheters were either not exercised or exercised to near exhaustion (mean run time of 102 \pm 13 min) before intravenous LPS challenge (1 mg/kg; lethality of dose is 10 - 20% in 24 h). Compared with time-matched nonexercised control rats, exercised rats had increased heart rates, plasma lactate, and plasma corticosterone and decreased plasma glucose at the conclusion of exercise. In response to LPS, both groups became hypotensive, exhibited transient hyperglycemia, and sustained hyperlactacidemia. By 30 min post-LPS, plasma corticosterone levels were similar in the two groups. Nonexercised rats exhibited a normal plasma TNF response to LPS with the peak value (10,400 \pm 2,000 U/ml) occurring 90 min after LPS challenge. In contrast, the TNF response in rats exercised before LPS administration was blunted to 17% of the nonexercised group, with the peak occurring at an earlier time after LPS. Addition of recombinant murine TNF to postexercise plasma

was fully expressed. The TNF response remained attenuated when LPS was administered up to 6 h after completion of exercise, but it returned to normal in rats allowed to recover for 24 h. The results demonstrate that exercise, perhaps as a stress modality, markedly suppresses the systemic TNF response that is normally observed in response to LPS challenge.

Author (Herner)

A95-75302

A BUOYANCY-DRIVEN SQUEEZE-FILM MODEL OF INTRAPLEURAL FLUID DYNAMICS: BASIC CONCEPTS

JAMES B. GROTEBERG Northwestern Univ., Evanston, IL, US and MATTHEW R. GLUCKSBERG Northwestern Univ., Evanston, IL, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1555-1561 Research sponsored by Whitaker Foundation

(Contract(s)/Grant(s): NIH-HL-01818; NIH-HL-41126; NSF CTS-90-13083)

(HTN-95-A0733) Copyright

We propose a new model of pleural liquid mechanics in the apneic animal based on the observation that the lung, in its position within the serious fluid of the chest, is a buoyant object with few physical connections to the chest. The buoyancy force due to the lung's low density causes the lung to rise within the chest, which in turn causes fluid to be squeezed out from the regions above the lung. The result is the transient component of the downward flow of intrapleural liquid and the less-than-hydrostatic vertical intrapleural pressure gradient observed by other investigators. For the purposes of mathematical simplicity, we have modeled the lung and chest wall of a horizontal animal as a pair of concentric cylinders separated by a narrow gap representing the pleural space. In this first version of the model, we treat the pleurae of the lung and chest wall as impermeable rigid boundaries, but despite these limitations, our mathematical analysis agrees with observations from a number of groups and explains the flow direction from top to bottom as well as the reported changes in vertical pressure gradient in response to a change in body orientation. Author (Herner)

A95-75303

MEASUREMENT OF HIGH VOLUMES BY NITROGEN WASHOUT METHOD

YAKOV SIVAN, JUERG HAMMER, and CHRISTOPHER J. L. NEWTH Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1562-1564

(HTN-95-A0734) Copyright

Studies in human infants suggested that thoracic gas volume (TGV) measured at end exhalation may not depict the true TGV and may differ from TGV measured from a series of higher lung volumes and corrected for the volume added. This was explained by gas trapping. If true, we should expect the discrepancy to be more pronounced when functional residual capacity (FRC) and higher lung volumes are measured by gas dilution techniques. We studied lung volumes above FRC by the nitrogen washout technique in 12 spontaneously breathing rhesus monkeys (5.0 - 11.3 kg wt; 42 compared measurements). Lung volumes directly measured were compared with preset lung volumes achieved by artificial inflation of the lungs above FRC with known volumes of air (100 - 260 ml). Measured lung volume strongly correlated with and was not significantly different from preset lung volume. The difference between measured and preset lung volume was 0 - 5% in 41 of 42 cases. The direction of the difference was unpredictable; in 22 of 42 cases the measured volume was larger than the preset volume, but in 17 of 42 cases it was smaller. The difference was not affected by the volume of gas artificially inflated into the lungs. We conclude that, overall, lung volumes above FRC can be reliably measured by the nitrogen washout technique and that FRC measurements by this method reasonably reflect true FRC.

Author (Herner)

A95-75304

SKELETAL MUSCLE GLUT-4 AND GLUCOSE UPTAKE DURING EXERCISE IN HUMANS

GLENN MCCONELL Royal Melbourne Hospital, Melbourne Univ., Parkville, Australia, MICHAEL MCCOY Royal Melbourne Hospital, Melbourne Univ., Parkville, Australia, JOSEPH PROIETTO Royal

Melbourne Hospital, Melbourne Univ., Parkville, Australia, and MARK HARGREAVES Royal Melbourne Hospital, Melbourne Univ., Parkville, Australia Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 3 September 1994 p. 1565-1568 Research sponsored by National Health and Medical Research Council of Australia and Diabetes Australia (HTN-95-A0735) Copyright

The present study examined the relationship between total skeletal muscle GLUT-4 protein level and glucose uptake during exercise. Eight active non-endurance-trained men cycled at 72 \pm 1% peak pulmonary oxygen consumption for 40 min, with rates of glucose appearance and disappearance (Rd) determined by utilizing a primed continuous infusion of (3-H-3) glucose commencing 2 h before exercise. Muscle glycogen content and utilization, citrate synthase activity, and total GLUT-4 protein were measured on muscle biopsy samples obtained from the vastus lateralis. A direct relationship existed between preexercise muscle glycogen content and glycogen utilization during exercise. Citrate synthase activity and glucose Rd at the end of exercise averaged 21.9 \pm 3.0 micromol/min/g and 27.3 \pm 2.5 micromol/kg/min, respectively. There was a direct correlation between citrate synthase activity and GLUT-4 protein, however, at the end of exercise, glucose Rd was inversely related to both GLUT-4 and citrate synthase activity. Plasma insulin, which decreased during exercise, was not related to glucose Rd. In conclusion, glucose uptake during 40 min of exercise at 72% peak pulmonary oxygen consumption was inversely related to the total muscle GLUT-4 protein level. This suggests that factors other than the total GLUT-4 protein level are important in the regulation of glucose uptake during exercise. Author (Hemer)

A95-76501

HOW B AND T CELLS TALK TO EACH OTHER

EDWARD A. CLARK Univ of Washington Medical Cent, Seattle, WA, United States and JEFFREY A. LEDBETTER Nature (ISSN 0028-0836) vol. 367, no. 6462 February 3, 1994 p. 425-428 refs (BTN-94-EIX94401310326) Copyright

The B cells of the immune system, which secrete antibodies against foreign antigens, are fully specific and effective only after maturation in lymph nodes and other lymphoid tissues. Immuno competent T cells play a crucial part in this process, but the molecular details of the way in which the two cell types interact have only recently become apparent. This paper summarizes some of the basic features of the T—B-cell dialog that have already emerged.

EI

A95-76502

PAIR-RULE EXPRESSION PATTERNS OF EVEN-SKIPPED ARE FOUND IN BOTH SHORT- AND LONG-GERM BEETLES

NIPAM H. PATEL Carnegie Inst of Washington, Baltimore, MD, United States, BARRY G. CONDRON, and KAI ZINN Nature (ISSN 0028-0836) vol. 367, no. 6462 February 3, 1994 p. 429-434 refs (BTN-94-EIX94401310327) Copyright

Now that the genes controlling embryonic patterning have been identified in several model organisms, long-standing questions concerning the evolution of developmental systems are open to investigation. Examination of the expression of even-skipped in a variety of insects reveals that insect germ-type designations apparently do not reflect the variations in the mechanisms of segmentation evident throughout insect phylogeny.

Author (EI)

A95-76505

SELF-ASSEMBLY OF A DOUBLE-HELICAL COMPLEX OF SODIUM

THOMAS W. BELL State Univ of New York, Stony Brook, NY, United States and HELENE JOUSSELIN Nature (ISSN 0028-0836) vol. 367, no. 6462 February 3, 1994 p. 441-444 refs (BTN-94-EIX94401310330) Copyright

Spontaneous self-organization of helical and multiple-helical molecular structures occurs on several levels in living organisms. We present an example of double-helical assembly induced by the weaker and non-directional interactions of an alkali-metal ion with an

organic ligand that is pre-organized into a coil. We have characterized the resulting complex by two-dimensional NMR and fast-atom-bombardment mass spectrometry. These results provide a step toward the creation of molecular tubes or ion channels consisting of intertwined coils.

Author (EI)

N95-22493# Iowa State Univ. of Science and Technology, Ames, IA.

DEVELOPMENT OF NOVEL SEPARATION TECHNIQUES FOR BIOLOGICAL SAMPLES IN CAPILLARY ELECTROPHORESIS

Ph.D. Thesis

HUAN-TSUNG CHANG 27 Jul. 1994 267 p

(Contract(s)/Grant(s): W-7405-ENG-82)

(DE95-001672; IS-T-1710) Avail: CASI HC A12/MF A03

This dissertation includes three different topics: general introduction of capillary electrophoresis (CE); gradient in CE and CE in biological separations; and capillary gel electrophoresis (CGE) for DNA separation. Factors such as temperature, viscosity, pH, and the surface of capillary walls affecting the separation performance are demonstrated. A pH gradient between 3.0 and 5.2 is useful to improve the resolution among eight different organic acids. A flow gradient due to the change in the concentration of surfactant, which is able to coat to the capillary wall to change the flow rate and its direction, is also shown as a good way to improve the resolution for organic compounds. A temperature gradient caused by joule heat is shown by voltage programming to enhance the resolution and shorten the separation time for several phenolic compounds. The author also shows that self-regulating dynamic control of electroosmotic flow in CE by simply running separation in different concentrations of surfactant has less matrix effect on the separation performance. One of the most important demonstrations in this dissertation is that the author proposes on-column reaction which gives several advantages including the use of a small amount of sample, low risk of contamination, and time saving and kinetic features. The author uses this idea with laser induced fluorescence (LIF) as a detection mode to detect an on-column digestion of subunit of protein. This technique also is applied to single cell analysis in the group.

DOE

N95-22588# Oak Ridge National Lab., TN. Bioprocessing Research and Development Center.

CONTINUOUS PRODUCTION OF CELLULASE IN A FLUIDIZED-BED REACTOR BY PSEUDONOMAS FLUORESCENS IMMOBILIZED IN HYDROGEL BEADS

JOHN M. COSGROVE, T. C. SCOTT, C. D. SCOTT, and H. C. DEES 1994 13 p Presented at the 16th Symposium on Biotechnology for Fuels and Chemicals, Gatlinburg, TN, 9-13 May 1994 (Contract(s)/Grant(s): DE-AC05-84OR-21400)

(DE94-014105; CONF-940526-6) Avail: CASI HC A03/MF A01

At present, the most widely used microorganism for commercial production of cellulase is probably the filamentous fungus *Trichoderma reesei*. The *T. reesei* cellulase system is typically complete and highly productive but the solid-state culture involves complex media and substrate and an inducer which add to the production costs. There is considerable interest in isolating bacteria that produce cellulase enzymes which are more stable, have higher temperature optima, and broader pH optima. Bacterial cellulases may also exhibit greater substrate specificity and more favorable reaction kinetics. We feel that enzyme production could be significantly enhanced by increasing the concentration of active biomass in the reactor, and using organisms that take advantage of simpler media or do not require inducers for enzyme production. Our efforts to develop a more effective cellulase production system have focused on a modified bacterium and on immobilization and utilization of the microorganism in a high-productivity fluidized-bed reactor. The approach is to use a proprietary, cellulase-producing pseudomonad-like bacterium under development at Oak Ridge National Laboratory. The cellulase is constitutively produced and excreted by the bacterium in a minimal media with no requirement for inducers or special chemicals. This bacterium is then immobilized in a hydrogel bead that is used in a continuous fluidized-bed

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bioreactor. The cellulase can be recovered in downstream processing of the bioreactor effluent. DOE

N95-22589# Department of Energy, Washington, DC. Office of Environment, Safety, and Health.
THE DEVELOPMENT AND APPLICATIONS OF BIOMARKERS
JANET NORMANDY, ed. and JOHN PEETERS, ed. 15 Apr. 1994
79 p Presented at the Workshop on Development and Application of Biomarkers, Santa Fe, NM, 26-29 Apr. 1994
(DE94-014249; DOE/EH-0377T; CONF-9404178-ABSTS) Avail: CASI HC A05/MF A01

This report is a compilation of submitted abstracts of scientific papers presented at the second Department of Energy-supported workshop on the use and applications of biomarkers held in Santa Fe, New Mexico, from April 26-29, 1994. The abstracts present a synopsis of the latest scientific developments in biomarker research and how these developments meet with the practical needs of the occupational physician as well as the industrial hygienist and the health physicist. In addition to considering the practical applications and potential benefits of this promising technology, the potential ethical and legal ramifications of using biomarkers to monitor workers are discussed. The abstracts further present insights on the present benefits that can be derived from using biomarkers as well as a perspective on what further research is required to fully meet the needs of the medical community. DOE

N95-22590# California Univ., Berkeley. Lawrence Berkeley Lab, CA. Structural Biology Div.
COMPARISON OF THE RATE CONSTANTS FOR ENERGY TRANSFER IN THE LIGHT-HARVESTING PROTEIN, C-PHYCOCYANIN, CALCULATED FROM FOERSTER'S THEORY AND EXPERIMENTALLY MEASURED BY TIME-RESOLVED FLUORESCENCE SPECTROSCOPY Ph.D. Thesis
MARTIN PAUL DEBRECZENY May 1994 168 p
(Contract(s)/Grant(s): DE-AC03-76SF-00098)
(DE94-014961; LBL-35672) Avail: CASI HC A08/MF A02

We have measured and assigned rate constants for energy transfer between chromophores in the light-harvesting protein C-phycocyanin (PC), in the monomeric and trimeric aggregation states, isolated from *Synechococcus* sp. PCC 7002. In order to compare the measured rate constants with those predicted by Foerster's theory of inductive resonance in the weak coupling limit, we have experimentally resolved several properties of the three chromophore types (beta(sub 155), alpha(sub 84), beta(sub 84)) found in PC monomers, including absorption and fluorescence spectra, extinction coefficients, fluorescence quantum yields, and fluorescence lifetimes. The cpcB/C155S mutant, whose PC is missing the beta(sub 155) chromophore, was useful in effecting the resolution of the chromophore properties and in assigning the experimentally observed rate constants for energy transfer to specific pathways. DOE

N95-22801*# Washington State Univ., Pullman, WA. Inst. of Biological Chemistry.
PLANT METABOLISM AND CELL WALL FORMATION IN SPACE (MICROGRAVITY) AND ON EARTH Progress Report
NORMAN G. LEWIS 1994 5 p
(Contract(s)/Grant(s): NAGW-3672)
(NASA-CR-197618; NAS 1.26:197618) Avail: CASI HC A01/MF A01

Variations in cell wall chemistry provide vascular plants with the ability to withstand gravitational forces, as well as providing facile mechanisms for correctional responses to various gravitational stimuli, e.g., in reaction wood formation. A principal focus of our current research is to precisely and systematically dissect the essentially unknown mechanism(s) of vascular plant cell wall assembly, particularly with respect to formation of its phenolic constituents, i.e., lignins and suberins, and how gravity impacts upon these processes. Formation of these phenolic polymers is of particular interest, since it appears that elaboration of their biochemical

pathways was essential for successful land adaptation. By extrapolation, we are also greatly intrigued as to how the microgravity environment impacts upon 'normal' cell wall assembly mechanisms/etabolism. Derived from text

N95-22866# Telluride Summer Research Center, Telluride, CO.
OPEN PROBLEMS OF COMPUTATIONAL MOLECULAR BIOLOGY
1993 68 p Presented at the 3d Computational Molecular Biology International Workshop, Telluride, CO, 11-25 Jul. 1993
(Contract(s)/Grant(s): DE-FG03-93ER-61638)
(DE95-000895; CONF-9307199-EXTD-ABSTS) Avail: CASI HC A04/MF A01 (US Sales Only)

This volume contains short papers and abstracts provided by session leaders of the Third International Workshop on Open Problems of Computational Molecular Biology held in Telluride, Colorado July 11 - 25, 1993. Individual contributions are abstracted and indexed for the database. DOE

N95-22872# Michigan Univ., Ann Arbor, MI. Dept. of Chemical Engineering.
BIOLOGICAL DETERMINANTS OF PHOTOBIOREACTOR DESIGN Quarterly Report No. 3, 1 Mar. - 31 May 1994
BERNHARD O. PALSSON and G. G. BROWN 1994 8 p
(Contract(s)/Grant(s): DE-FG22-93PC-93212)
(DE94-016032; DOE/PC-93212/T3) Avail: CASI HC A02/MF A01

Proper mixing is very important for achieving high concentration photosynthetic cultures. Good mixing can keep the cells in suspension, eliminate thermal stratification, help nutrient distribution, and improve gas exchange. We have tested various configurations of photobioreactors and found a PBR with a vertical rectangular slab-shaped illumination chamber to be the best. This shape meets all the criteria of a successful photobioreactor and could support *Chlorella vulgaris* up to 10(exp 8) cells/ml. DOE

N95-22873# Ohio State Univ., Columbus, OH. Dept. of Microbiology.
TRANSMETHYLATION REACTIONS DURING METHANOGENESIS FROM ACETATE IN METHANOSARCINA BARKERI Annual Technical Progress Report, Aug. 1993 - Jul. 1994

JOSEPH A. KRZYCKI 1994 22 p
(Contract(s)/Grant(s): DE-FG02-91ER-20042)
(DE94-016222; DOE/ER-20042/2) Avail: CASI HC A03/MF A01

Catabolic production of methane by methanogenic archaeobacteria is a unique biochemical process, employing several unusual cofactors and a variety of unusual enzymes. *Methanosarcina barkeri* MS (DSM 800) metabolizes H₂/CO₂, methanol, monomethylamine (MMA), dimethylamine (DMA), and trimethylamine (TMA), and acetate. *M. barkeri* possesses multiple methyltransferases which convert methylated substrates to methylated cofactors or proteins prior to their reduction to methane. Methylated substrates are also oxidized to CO₂ to provide reducing equivalents for reduction to methane or for biosynthesis. This short review focuses on methyltransferase reactions leading to methane formation in *Methanosarcina*. DOE

N95-22874# University of Southern Illinois, Carbondale, IL. Dept. of Microbiology.
REGULATION OF ALCOHOL FERMENTATION IN ESCHERICHIA COLI Progress Report, Jul. 1991 - Jun. 1994
DAVID P. CLARK 1994 7 p
(Contract(s)/Grant(s): DE-FG02-88ER-13941)
(DE94-016227; DOE/ER-13941/5) Avail: CASI HC A02/MF A01

This report describes progress in sections entitled (1) Regulation of the adhE gene, (2) Molecular Analysis of the adhE Promoter Region, (3) The adhR Regulatory System, (4) The Molecular Biology of the AdhE Protein, (5) The Fermentative Lactate Dehydrogenase, (6) A Novel Secondary ADH from *Salmonella*, (7) Regulation of the cadA gene, and (8) Side Issues. DOE

N95-22884# Wisconsin Univ., Madison, WI.
**ANALYSIS OF STRUCTURAL DOMAINS REQUIRED FOR
 PHYTOCHROME FUNCTION BY IN VITRO MUTAGENESIS**
 Progress Report, 1993 - 1994

RICHARD D. VIERSTRA 1994 3 p
 (Contract(s)/Grant(s): DE-FG02-88ER-13968)
 (DE94-016230; DOE/ER-13968/3) Avail: CASI HC A01/MF A01

We have successfully expressed in tobacco a series of 8 nested deletions of phytochrome A that involved the removal of both amino- and carboxy-terminal sequences. From examination of the encoded proteins synthesized in plants, we have identified several domains important for phytochrome structure and function. Sequences necessary for chromophore attachment in vivo were localized to the amino-terminal 398 residues because mutant proteins this small had covalently bound chromophore. Deletion mutants from the carboxy terminus to residue 653 were spectrally indistinguishable from the full-length chromoprotein. In contrast, further truncation to residue 399 resulted in a chromoprotein with a bleached Pfr absorbance spectrum; Pr and Pfr absorbance maxima shifted toward shorter wavelengths; and reduced Pfr to Pr phototransformation efficiency. These results identified residues between 399 and 652 as essential for spectral integrity, but are not essential for chromophore attachment. Sequence(s) between residues 919 and 1093 appear to be necessary for dimerization. Carboxy-terminal mutants containing this region behaved as dimers under nondenaturing conditions in-vitro, whereas truncations without this region behaved as monomers. DOE

N95-22890# Oak Ridge National Lab., TN. Informatics Group.
**AN IMPROVED SYSTEM FOR EXON RECOGNITION AND
 GENE MODELING IN HUMAN DNA SEQUENCES**

YING XU, J. RALPH EINSTEIN, R. J. MURAL, MANESH SHAH, and E. C. UBERBACHER 1994 14 p. Presented at the 2nd International Conference on Intelligent Systems for Molecular Biology, Stanford, CA, 15-17 Aug. 1994
 (Contract(s)/Grant(s): DE-AC05-84OR-21400)
 (DE94-017863; CONF-9408117-3) Avail: CASI HC A03/MF A01

A new version of the GRAIL system called GRAIL II, has recently been developed. GRAIL II is a hybrid artificial intelligence system that supports a number of DNA sequence analysis tools including protein-coding region recognition. PolyA site and transcription promoter recognition, gene model construction, translation to protein, and DNA/protein database searching capabilities. This paper describes the core of GRAIL II, the coding exon recognition and gene model construction algorithms. The exon recognition algorithm recognizes coding exons by combining coding feature analysis and edge-signal (acceptor/donor/translation-start sites) detection. Unlike the original GRAIL system, this algorithm uses variable-length windows tailored to each potential exon candidate, making its performance almost exon length-independent. In this algorithm, the recognition process is divided into four steps. Initially a large number of possible coding exon candidates are generated. Then a rule-based prescreening algorithm eliminates the majority of the improbable candidates. As the kernel of the recognition algorithm, three neural networks are trained to evaluate the remaining candidates. The outputs of the neural networks are then divided into clusters of candidates, corresponding to presumed exons. The algorithm makes its final prediction by picking the best candidate from each cluster. The gene construction algorithm uses a dynamic programming approach to build gene models by using as input the clusters predicted by the exon recognition algorithm. DOE

N95-22897# Stanford Linear Accelerator Center, CA.
**PROTEIN FOLDING AND PROTEIN METALLOCLUSTER
 STUDIES USING SYNCHROTRON SMALL ANGLE X RAY
 SCATTERING** Ph.D. Thesis

DAVID ELIEZER Jun. 1994 162 p
 (Contract(s)/Grant(s): DE-AC03-76SF-00515)
 (DE95-003339; SU-SLAC-448) Avail: CASI HC A08/MF A02

Proteins, biological macromolecules composed of amino-acid building blocks, possess unique three dimensional shapes or con-

formations which are intimately related to their biological function. All of the information necessary to determine this conformation is stored in a protein's amino acid sequence. The problem of understanding the process by which nature maps protein amino-acid sequences to three-dimensional conformations is known as the protein folding problem, and is one of the central unsolved problems in biophysics today. The possible applications of a solution are broad, ranging from the elucidation of thousands of protein structures to the rational modification and design of protein-based drugs. The scattering of x rays by matter has long been useful as a tool for the characterization of physical properties of materials, including biological samples. The high photon flux available at synchrotron x ray sources allows for the measurement of scattering cross-sections of dilute and/or disordered samples. Such measurements do not yield the detailed geometrical information available from crystalline samples, but do allow for lower resolution studies of dynamical processes not observable in the crystalline state. The main focus of the work described here has been the study of the protein folding process using time-resolved small-angle x ray scattering measurements. The original intention was to observe the decrease in overall size which must accompany the folding of a protein from an extended conformation to its compact native state. Although this process proved too fast for the current time-resolution of the technique, upper bounds were set on the probable compaction times of several small proteins. In addition, an interesting and unexpected process was detected, in which the folding protein passes through an intermediate state which shows a tendency to associate. This state is proposed to be a kinetic molten globule folding intermediate. DOE

N95-22911*# Alabama A & M Univ., Normal, AL. Dept. of Biology.
GENETIC EFFECTS ON HEAVY IONS IN DROSOPHILA Final
 Technical Report

P. G. KALE 1986 22 p
 (Contract(s)/Grant(s): NAG9-246)
 (NASA-CR-197916; NAS 1.26:197916) Avail: CASI HC A03/MF A01

Drosophila sex-linked recessive lethal mutation test was used to study the dose response relation and relative biological effectiveness of heavy ions. The experiments were performed using the heavy ion beams at BEVALAC of Lawrence Berkeley Laboratory. These experiments were undertaken according to the proposed milestones and included Ne-20, A-40 and Fe-65 ions with respective energies of 600 MeV, 840 MeV and 850 MeV. At these energies several doses of these radiations ranging from 20 to 1280 R were used. Space radiation exposure to astronauts is supposed to be quite low and therefore very low dose experiments i.e., 20 R, were also performed for the three ions. The mutation response was measured in all germ cell types i.e., spermatozoa, spermatids, spermatocytes and spermatogonia of treated *Drosophila* males. A linear dose frequency relation was observed for most of the range except at high doses where the saturation effect was observed. Also, a very significant difference was observed among the sensitivity of the four germ cell stages where spermatozoa and spermatids were more sensitive. At the higher doses of this range, most of the spermatogonia and spermatocytes were killed. Although comparative and identical experiments with X-rays or neutrons have not been performed, the comparison of our data with the ones available in literature suggest that the heavy ions have a high rbe and that they are several times more effective than low LET X-rays. The rbe compared to neutrons however appears to be only slightly higher. Author

N95-22912# Argonne National Lab., IL. Biological and Medical Research Div.

**ACTIVATION OF THE JUN-D GENE IN HUMAN MYELOID
 CELLS BY 1-(BETA)-D-ARABINOFURANOSYLCYTOSINE**
 SURENDER KHARBANDA (Harvard Medical School, Boston, MA.), DONALD KUFE (Harvard Medical School, Boston, MA.), and ELIEZER HUBERMAN (Harvard Medical School, Boston, MA.)
 1994 21 p

(Contract(s)/Grant(s): W-31-109-ENG-38)

(DE94-016591; ANL/BIM/PP-76678) Avail: CASI HC A03/MF A01

The transcription factor AP-1 binds to a DNA consensus sequence TGA(sup G)/(sub C)TCA (TRE) that regulates the activation of genes responsive to phorbol esters. This factor is a complex composed of proteins encoded by different members of the jun and fos gene family. The c-jun gene, which is induced as an immediate early event by phorbol esters, as well as serum and growth factors, codes for a major form of AP-1. The c-jun, jun-B and jun-D genes are differentially expressed in mouse tissues. jun-D mRNA is more abundant than c-jun and, while jun-B and jun-D expression is similar in most tissues, jun-B mRNA levels are higher than that for jun-D in testis and ovary. Levels of jun-D expression are also higher compared to c-jun and jun-B in quiescent 3T3 cells. Moreover, while c-jun and jun-B transcription is stimulated by phorbol esters and, serum, similar conditions have minimal effects on jun-D expression. These findings have suggested that the jun-D gene has a distinct role in control of gene activity. The treatment of human myeloid leukemia cells with ara-C is associated with transient increases in c-jun and jun-B gene expression. However, transcriptional activation of the c-jun and jun-B genes and the mechanisms responsible for these effects remain unclear. The present studies extend these findings to the jun-D gene. The results demonstrate that ara-C increases jun-D expression by both transcriptional and posttranscriptional mechanisms. We also demonstrate that this agent has little effect on expression of genes coding for proteins that bind to the related cAMP-responsive consensus sequence. DOE

N95-22913# Argonne National Lab., IL. Center for Mechanistic Biology and Biotechnology.

REARRANGEMENT OF RAG-1 RECOMBINASE GENE IN RADIATION-SENSITIVE WASTED MICE

GAYLE E. WOLOSCHAK, CLAUDIA R. LIBERTIN (Loyola Univ., Chicago, IL.), PAUL WEAVER, MARK CHURCHILL, and CHIN-MEI CHANG-LIU 1994 22 p

(Contract(s)/Grant(s): W-31-109-ENG-38)

(DE94-017083; ANL/CMB/PP-82201) Avail: CASI HC A03/MF A01

The recent cloning and characterization of recombinase genes (RAG-1/RAG-2) expressed in lymphoid and possibly central nervous system tissues prompted us to examine expression of these genes in DNA repair-deficient/immunodeficient wasted mice (wst). Our results revealed expression of RAG-1 mRNA was detected in spinal cord or brain from wst/wst mice or their normal littermates (wst/(sm bullet)mice). In thymus tissue, a small RAG-1 transcript was detected in wst/wst mice that was not evident in thymus from control mice. In wst/(lg bullet) mice, a two-fold increase in RAG-1 mRNA was evident in thymus tissue. RAG-2 mRNA could only be detected in thymus tissue from wst/(sm bullet) and not from wst/wst or parental control BCF(sub 1) mice. Southern blots revealed a rearrangement/deletion within the RAG-1 gene of affected wasted mice, not evident in known strain-specific parental or littermate controls. These results support the idea that the RAG-1 gene may map at or near the locus for the wasted mutation. In addition, they suggest the importance of recombinase function in normal immune and central nervous system development as well as the potential contribution of this gene family to the normal repair of radiation-induced DNA damage. DOE

N95-22963*# Universidade Estadual de Paulista, Sao Paulo (Brazil).

A SUPERSYMMETRIC FAMILY OF HARMONIC OSCILLATORS SIMULATING H-BONDS IN DNA

ELSO DRIGO FILHO and JOSE R. RUGGIERO *In* NASA. Goddard Space Flight Center, Second International Workshop on Harmonic Oscillators p 45-49 Jan. 1995 Sponsored by CNPq and FAPESP Avail: CASI HC A01/MF A04

We test an isospectral potential from harmonic oscillator simulating H-bond interaction in DNA macromolecules. Author

N95-23050# International Centre for Theoretical Physics, Trieste (Italy).

MEMBRANE PHASE SEPARATIONS, ASYMMETRY AND IMPLICATIONS IN THE ORIGIN OF LIFE

M. O. EZE Nov. 1993 8 p

(DE94-628486; IC-93/381) Avail: CASI HC A02/MF A01 (US Sales Only)

Membrane lipids, by affecting membrane physical state, influence solute transport as in *Escherichia coli*, and play a prominent role in homeoviscous (homeophasic) adaptation whereby cells adapt to varying temperatures. Thus, on prebiotic earth, lipid-doped precells were possibly stabilized. Studies to investigate this hypothesis are advocated. DOE

N95-23053# International Centre for Theoretical Physics, Trieste (Italy).

ENHANCEMENT OF BIOMEMBRANE FUNCTIONS UNDER PHASE-SEPARATED CONDITIONS: A SELF-ORGANIZED CRITICALITY PHENOMENON?

M. O. EZE and J. CHELAFLORES Dec. 1993 8 p

(DE94-628489; IC-93/398) Avail: CASI HC A02/MF A01 (US Sales Only)

Self-organized criticality (SOC) is hereby proposed as a possible physical basis for explaining observations in the temperature-dependence of the rates of biological membrane-associated events. The biomembrane undergoes a reversible, cooperative, thermotropic gel-to-liquid crystalline phase transition which is broad, and involves lateral phase separation. The lateral phase separated (rather than the totally gel-, or the totally liquid crystalline-) membrane state has been observed to be the state in which vital membrane functions are facilitated. The membrane in this unique state is viewed, for our purposes here, as a dynamical, extended dissipative system with spatial and temporal degrees of freedom, exhibiting power law behavior, typical of the self-organized critical state. Experiments are suggested for verifying this hypothesis. DOE

N95-23058# International Centre for Theoretical Physics, Trieste (Italy).

THE ORIGIN OF CHIRALITY IN PROTEIN AMINO ACIDS

J. CHELAFLORES Mar. 1994 13 p

(DE94-628491; IC-94/59) Avail: CASI HC A03/MF A01 (US Sales Only)

We discuss the origin of the chirality of protein amino acids from the point of view of a phase transition from a racemic mixture into an optically pure state. We assume that Bose-Einstein condensation may act as an amplification mechanism. The original theory is due to Salam. We suggest a new role for the phase transition. Following Quack we distinguish parity violation of two kinds (de facto and de lege symmetry breaking). While the Salam phase transition corresponds to parity violation of the second kind (de lege), the phase transition we discuss in this work corresponds to parity violation of what we may call a third kind. This is suggested by recent experimental phenomena which correlate chiral symmetry breaking and pattern formation (spontaneous symmetry breaking that separates an initial racemic mixture into right- and left-handed space domains by means of a substrate). Tentative comments are given on the eventual design of possible experiments that may test this new hypothesis. DOE

N95-23060# International Centre for Theoretical Physics, Trieste (Italy).

MOLECULAR RELICS FROM CHEMICAL EVOLUTION AND THE ORIGIN OF LIFE

J. CHELAFLORES Apr. 1994 16 p

(DE94-628493; IC-94/75) Avail: CASI HC A03/MF A01 (US Sales Only)

The main hypothesis proposed in this work intends to remove the difficulty that arises from the conjecture that the RNA world may have left molecular relics that may still be extant in the angiosperms. We discuss whether it is possible to envisage a possible evolutionary pathway of the RNA replicators spanning the vast time span separating the first appearance of the angiosperms, late in the Mesozoic era (the Lower Cretaceous), from the most likely suberas in which the RNA world may have occurred, namely the Hadean/

Early Archean. In order to address this question we suggest that through horizontal gene transfer, as well as through a series of symbiosis of the precursor cell of the land plants, the genes of the replicases (RNA-directed RNA polymerases) associated with putative DNA-independent RNA replicators may have been transferred vertically, eventually becoming specific to the angiosperms. DOE

N95-23177*# National Aeronautics and Space Administration. Lewis Research Center, Cleveland, OH.

NASA ADVANCED REFRIGERATOR/FREEZER TECHNOLOGY DEVELOPMENT PROJECT OVERVIEW

J. E. CAIRELLI Mar. 1995 10 p Presented at the 8th International Cryocooler Conference, Vail, CO, 28-30 Jun. 1994; sponsored by the ICC Conference Committee

(Contract(s)/Grant(s): RTOP 233-03-0A)

(NASA-TM-106309; E-9204; NAS 1.15:106309) Avail: CASI HC A02/MF A01

NASA Lewis Research Center (LeRC) has recently initiated a three-year project to develop the advanced refrigerator/freezer (R/F) technologies needed to support future life and biomedical sciences space experiments. Refrigerator/freezer laboratory equipment, most of which needs to be developed, is enabling to about 75 percent of the planned space station life and biomedical science experiments. These experiments will require five different classes of equipment; three storage freezers operating at -20 C, -70 C and less than 183 C, a -70 C freeze-dryer, and a cryogenic (less than 183 C) quick/snap freezer. This project is in response to a survey of cooling system technologies, performed by a team of NASA scientists and engineers. The team found that the technologies, required for future R/F systems to support life and biomedical sciences spaceflight experiments, do not exist at an adequate state of development and concluded that a program to develop the advanced R/F technologies is needed. Limitations on spaceflight system size, mass, and power consumption present a significant challenge in developing these systems. This paper presents some background and a description of the Advanced R/F Technology Development Project, project approach and schedule, general description of the R/F systems, and a review of the major R/F equipment requirements. Author

N95-23251 Army Natick Labs., MA.

EFFECT OF HYPERBARIC CARBON DIOXIDE ON SPORES AND VEGETATIVE CELLS OF BACILLUS

STEAROTHERMOPHILUS Final Report, 30 Mar. - 30 Sep. 1992

CHESTER T. ROSKEY and ANTHONY SIKES May 1994 36 p Limited Reproducibility: More than 20% of this document may be affected by microfiche quality

(AD-A280115; NATICK/TR-94/019) Avail: CASI HC A03

Spore suspensions in water, 0.05M pH 7 phosphate buffer, 0.05M pH 4.5 and 0.05M pH 4.0 acetate buffer, and antibiotic assay media supplement broth (AAMS) were subjected to 50 psi to 1100 psi carbon dioxide at various temperatures in Parr bombs for up to 96 hours. Spores were resistant to high pressure carbon dioxide treatment at each pH and at both high and low temperatures. Spore suspensions that were first heat activated and then incubated at 550C for a short time increased sensitivity to destruction by CO₂. Although spores were resistant to destruction by hyperbaric CO₂ low pressure (50 psi) CO₂ was seen to completely inhibit spore germination and outgrowth. Inhibition to germination was found to be reversible. Spore germination was found to be impaired in carbonated AAMS broth. However, the addition of 50 mM NaHCO₃ to AAMS enhanced germination and outgrowth. DTIC

N95-23771# Argonne National Lab., IL. Biological and Medical Research Div.

A COMPARATIVE STUDY OF THE EFFECTS OF CLOFIBRATE, CIPROFIBRATE, WY-14,643, AND DI-(2-ETHYLHEXYL)-PHthalate ON LIVER PROTEIN EXPRESSION IN MICE

CAROL S. GIOMETTI, JOHN TAYLOR, M. ANNE GEMMELL,

SANDRA L. TOLLAKESEN, NARENDRA D. LALWANI (Northwestern Univ., Chicago, IL.), and JANARDAN K. REDDY (Northwestern Univ., Chicago, IL.) 1994 17 p

(Contract(s)/Grant(s): W-31-109-ENG-38)

(DE94-016587; ANL/BIM/PP-71687) Avail: CASI HC A03/MF A01

A comparative study of the effects of clofibrate, ciprofibrate, WY-14,643, and di-(2-ethylhexyl)-phthalate on liver protein expression in mice is described. Two-dimensional gel electrophoresis (2DE) coupled with computer-assisted data analysis was used to examine liver protein expression in untreated mice and in mice exposed to 0.25% clofibrate, 0.025% ciprofibrate, 0.1% (4-chloro-6(2,3-xylidino)-2-pyrimidinylthio)acetic acid (Wy-14,643), or 2.0% di-(2-ethylhexyl)-phthalate (DEHP). To determine the subcellular distribution of the proteins seen in 2DE patterns of liver, preparations of mitochondria, microsomes, peroxisomes, and cytosol were also analyzed by 2DE. At the doses administered, all of these chemicals are known to cause comparable levels of peroxisome proliferation accompanied by an increase in betaoxidation of lipids, and upon prolonged administration, hepatocellular carcinoma. The similarities in biological effects suggest a pleiotropic biochemical response to this group of chemicals. Analysis of 2DE patterns of liver proteins showed that 260 proteins out of a total of approximately 400 were changed in abundance by at least one of the four treatments used. Out of these 260 quantitative protein changes, 45 were comparable in magnitude and direction for all four treatments while the remainder showed treatment-related variability in either magnitude or direction of response. These results indicate, therefore, that against a background of protein changes that are characteristic of the individual chemicals, there is a set of pleiotropic protein changes common to the peroxisome proliferators. The subcellular location of the proteins involved in this pleiotropic response does not appear to be restricted to the peroxisome fraction. DOE

N95-23821*# Morgan State Univ., Baltimore, MD.

GERMINATION, GROWTH RATES, AND ELECTRON MICROSCOPE ANALYSIS OF TOMATO SEEDS FLOWN ON THE LDEF

ERNEST C. HAMMOND, JR., KEVIN BRIDGERS, and CECILIA WRIGHT BROWN In NASA. Langley Research Center, LDEF: 69 Months in Space. Third Post-Retrieval Symposium, Part 1 p 231-252 Feb. 1995

Avail: CASI HC A03/MF A04

The tomato seeds were flown in orbit aboard the Long Duration Exposure Facility (LDEF) for nearly six years. During this time, the tomato seeds received an abundant exposure to cosmic radiation and solar wind. Upon the return of the LDEF to earth, the seeds were distributed throughout the United States and 30 foreign countries for analysis. The purpose of the experiment was to determine the long term effect of cosmic rays on living tissue. Our university analysis included germination and growth rates as well as Scanning Electron Microscopy and X-ray analysis of the control as well as Space-exposed tomato seeds. In analyzing the seeds under the Electron Microscope, usual observations were performed on the nutritional and epidermis layer of the seed. These layers appeared to be more porous in the Space-exposed seeds than on the Earth-based control seeds. This unusual characteristic may explain the increases in the space seeds growth pattern. (Several test results show that the Space-exposed seeds germinate sooner than the Earth-Based seeds. Also, the Space-exposed seeds grew at a faster rate). The porous nutritional region may allow the seeds to receive necessary nutrients and liquids more readily, thus enabling the plant to grow at a faster rate. Roots, leaves and stems were cut into small sections and mounted. After sputter coating the specimens with Argon/Gold Palladium Plasma, they were ready to be viewed under the Electron Microscope. Many micrographs were taken. The X-ray analysis displayed possible identifications of calcium, potassium, chlorine, copper, aluminum, silicon, phosphate, carbon, and sometimes sulfur and iron. The highest concentrations were shown in potassium and calcium. The Space-exposed specimens displayed a high concentration of copper and calcium in the two specimens. There

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was a significantly high concentration of copper in the Earth-based specimens, whereas there was no copper in the Space-exposed specimens. Author

N95-24047* Rhode Island Univ., Kingston, RI.
THE 1993 GORDON RESEARCH CONFERENCE ON CHRONOBIOLOGY Final Report
WILLIAM J. SCHWARTZ 1993 41 p Conference held in New London, NH, 9-13 Aug. 1993
(Contract(s)/Grant(s): NAGW-3645)
(NASA-CR-197990; NAS 1.26:197990) Avail: CASI HC A03/MF A01

The study of biological timekeeping is now at a particularly fertile stage, encompassing multiple levels of biological organization, recruiting a wide array of disciplines and methodologies and uniting a host of investigators. This report summarizes a research conference on Chronobiology. Some of the topics focused on transcriptional and translational mechanisms of circadian rhythmicity, with discussions of putative 'clock genes' in cyanobacteria, algae, fungi, fruitflies, and hamsters. Cellular analysis, with emphasis on photoreceptors in frogs, neurons in molluscs, and testis in moths was addressed. New methods for investigating the circadian clock in the suprachiasmatic nucleus were introduced.

Derived from text

N95-24075# Georgia Univ., Athens, GA.
STRUCTURAL STUDIES OF COMPLEX CARBOHYDRATES OF PLANT CELL WALLS Final Report, 15 Dec. 1989 - 14 Jun. 1993

A. G. DARVILL Oct. 1994 16 p
(Contract(s)/Grant(s): DE-FG09-85ER-13426)
(DE95-003099; DOE/ER-13426/T3) Avail: CASI HC A03/MF A01

Characterizing the polysaccharides that constitute the primary cell walls of plants and developing the methods for these characterizations has been a major research goal of our laboratory for many years. We have made considerable progress in both of these areas during the past three years. The cell walls of a plant determine the plant's structure and morphology and act as a barrier to pests. Cell walls also control the rate of growth of plant cells and are a source of complex carbohydrates with biological regulatory properties (oligosaccharins). The research projects supported by this grant concentrate on the isolation and structural characterization of the complex carbohydrates that account for approximately 70-80% of the primary cell walls of dicotyledons and non-graminaceous monocotyledons. Abstracts of papers published, in press, or in preparation reporting work supported by this grant during the past three years follow and summarize more fully the progress made in this research project. DOE

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AEROSPACE MEDICINE

Includes physiological factors; biological effects of radiation; and effects of weightlessness on man and animals.

A95-74354* National Aeronautics and Space Administration.
Lyndon B. Johnson Space Center, Houston, TX.

SPACEFLIGHT ALTERS AUTONOMIC REGULATION OF ARTERIAL PRESSURE IN HUMANS

JANICE M. FRITSCH-YELLE, JOHN B. CHARLES, MICHELE M. JONES, LARRY A. BEIGHTOL, and DWAIN L. ECKBERG Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 1776-1783 Research sponsored by Dept. of Veterans Affairs
(Contract(s)/Grant(s): NAS9-17720; NAS9-16038; NAG2-408; NIH-HL-22296)
(HTN-95-A0653) Copyright

Spaceflight is associated with decreased orthostatic tolerance

after landing. Short-duration spaceflight (4 - 5 days) impairs one neutral mechanism: the carotid baroreceptor-cardiac reflex. To understand the effects of longer-duration spaceflight on baroreflex function, we measured R-R interval power spectra, antecubital vein plasma catecholamine levels, carotid baroreceptor-cardiac reflex responses, responses to Valsalva maneuvers, and orthostatic tolerance in 16 astronauts before and after shuttle missions lasting 8 - 14 days. We found the following changes between preflight and landing day: (1) orthostatic tolerance decreased; (2) R-R interval spectral power in the 0.05- to 0.15-Hz band increased; (3) plasma norepinephrine and epinephrine levels increased; (4) the slope, range, and operational point of the carotid baroreceptor cardiac reflex response decreased; and (5) blood pressure and heart rate responses to Valsalva maneuvers were altered. Autonomic changes persisted for several days after landing. These results provide further evidence of functionally relevant reductions in parasympathetic and increases in sympathetic influences on arterial pressure control after spaceflight.

Author (Hemer)

A95-74377* National Aeronautics and Space Administration.
Lyndon B. Johnson Space Center, Houston, TX.

LUNG VOLUMES DURING SUSTAINED MICROGRAVITY ON SPACELAB SLS-1

ANN R. ELLIOTT California Univ., San Diego, La Jolla, CA, US, G. KIM PRISK California Univ., San Diego, La Jolla, CA, US, HAROLD J. B. GUY California Univ., San Diego, La Jolla, CA, US, and JOHN B. WEST California Univ., San Diego, La Jolla, CA, US Journal of Applied Physiology (ISSN 8750-7587) vol. 77, no. 4 October 1994 p. 2005-2014

(Contract(s)/Grant(s): NAS9-16037)
(HTN-95-A0676) Copyright

Gravity is known to influence the mechanical behavior of the lung and chest wall. However, the effect of sustained microgravity (microgravity) on lung volumes has not been reported. Pulmonary function tests were performed by four subjects before, during, and after 9 days of microgravity exposure. Ground measurements were made in standing and supine postures. Tests were performed using a bag-in-box-and-flowmeter system and a respiratory mass spectrometer. Measurements included functional residual capacity (FRC), expiratory reserve volume (ERV), residual volume (RV), inspiratory and expiratory vital capacities (IVC and EVC), and tidal volume (V_{sub T}). Total lung capacity (TLC) was derived from the measured EVC and RV values. With preflight standing values as a comparison, FRC was significantly reduced by 15% (approximately 500 ml) in microgravity and 32% in the supine posture. ERV was reduced by 10 - 20% in microgravity and decreased by 64% in the supine posture. RV was significantly reduced by 18% (310 ml) in microgravity but did not significantly change in the supine posture compared with standing. IVC and EVC were slightly reduced during the first 24 h of microgravity but returned to 1-G standing values within 72 h of microgravity exposure. IVC and EVC in the supine posture were significantly reduced by 12% compared with standing. During microgravity, V_{sub T} decreased by 15% (approximately 90 ml), but supine V_{sub T} was unchanged compared with preflight standing values. TLC decreased by approximately 8% during microgravity and in the supine posture compared with preflight standing. The reductions in FRC, ERV, and RV during microgravity are probably due to the cranial shift of the diaphragm, an increase in intrathoracic blood volume, and more uniform alveolar expansion.

Author (Hemer)

A95-75510

DYNAMICAL THERMOVISION FOR A STUDY OF BLOOD FLOW REGULATION AND PATHOLOGIES

A. G. MARKOV, L. G. KORENEVA, and A. V. PETROV Radiotekhnika i Elektronika (ISSN 0033-8494) vol. 39, no. 5 May 1994 p. 841-850 In RUSSIAN refs

(BTN-94-EIX94401361400) Copyright

The methods for obtaining information from bio-object surface temperature dynamics are described. Different factors forming

these dynamics are discussed. The main contribution of the surface blood flow to the depth of several millimeters is noted. Some transients are described and the observed temperature changes nature is discussed. Examples of the dynamic changes are given for the cases of pathology. EI

N95-22770 Institut National de la Sante et de la Recherche Medicale, Bordeaux (France).

INTERRELATIONS BETWEEN NERVOUS SYSTEM AND IMMUNE SYSTEM IN STRESS SITUATIONS Final Report, 1 Jan. 1991 - 31 Dec. 1992 [INTER-RELATIONS ENTRE SYSTEME NERVEUX ET SYSTEME IMMUNITAIRE DANS LES SITUATIONS DE STRESS]

R. DANTZER and G. SIMONNET 25 Mar. 1994 21 p In FRENCH (PB95-135521) Avail: Issuing Activity (National Technical Information Service (NTIS))

Designed to define the interrelations between the nervous system and the immune system in stress situations, the research covered by the contract involved a study of the behavioral and physic effects of the cytokines released by immune cells during infection and inflammation, and of the role of anti-morphinic peptides in maintaining homeostasis in disrupted situations. The results obtained show the importance of functional peptide/antipeptide couples in regulating the various phases of adjustment to stress (defense and recovery). NTIS

N95-22875# New England Medical Center Hospitals, Boston, MA. **CONTINUATION OF BNCT RESEARCH PROGRAM AT NEMC AND MIT Technical Progress Report, 1 Jun. 1993 - 31 May 1994**

ROBERT G. ZAMENHOF (Massachusetts Inst. of Tech., Cambridge, MA.) 1 Jul. 1994 13 p (Contract(s)/Grant(s): DE-FG02-87ER-60600) (DE94-016228; DOE/ER-60600/4) Avail: CASI HC A03/MF A01

We report on a complete state of readiness for initiating clinical trials of boron neutron capture therapy (BNCT). We present a summary of the status of our program in the context of our being the first research group in the US to have achieved a state of readiness to initiate clinical trials of BNCT. Topics covered in this summary includes: High-Resolution Alpha-Autoradiography; Design of a Final Optimized Epithermal Neutron Beam for Clinical Studies; Preliminary Design of a Fission Converter Epithermal Beam; Dosimetry and Treatment Planning Using Monte Carlo; Microdosimetry of the B-10 Reaction; Prompt-Gamma B-10 Analysis Facility; Experimental In-Phantom Dosimetry; Development of a Dose Control System in the Medical Room Development of Patient Support System in Medical Room; Development of Patient Positioning System in Medical Room; General Upgrades to Medical Therapy Room; Evaluation of Collateral Dose to Irradiated Patients; Design of Clinical Phase-I Melanoma and Glioblastoma Study; Approvals for Phase-I Melanoma and Glioblastoma Studies; Other Research Activities in Neutron Capture Therapy; and Training of NEMC and MIT Staff for Clinical Studies. DOE

N95-22987*# Universidad Nacional Autonoma de Mexico, Cuernavaca (Mexico). Lab. de Cibernetica.

NEURODYNAMIC OSCILLATORS

ISMAEL ESPINOSA, HORTENSIA GONZALEZ, JORGE QUIZA, J. JESUS GONZALEZ, RUBEN ARROYO, and RITALUZ LARA (Instituto Politecnico Nacional, Mexico City, Mexico.) In NASA. Goddard Space Flight Center, Second International Workshop on Harmonic Oscillators p 255-262 Jan. 1995 Sponsored by Direccion General de Asuntos del Personal Academico Avail: CASI HC A02/MF A04

Oscillation of electrical activity has been found in many nervous systems, from invertebrates to vertebrates including man. There exists experimental evidence of very simple circuits with the capability of oscillation. Neurons with intrinsic oscillation have been found and also neural circuits where oscillation is a property of the network. These two types of oscillations coexist in many instances. It is nowadays hypothesized that behind synchronization and oscillation

there is a system of coupled oscillators responsible for activities that range from locomotion and feature binding in vision to control of sleep and circadian rhythms. The huge knowledge that has been acquired on oscillators from the times of Lord Rayleigh has made the simulation of neural oscillators a very active endeavor. This has been enhanced with more recent physiological findings about small neural circuits by means of intracellular and extracellular recordings as well as imaging methods. The future of this interdisciplinary field looks very promising; some researchers are going into quantum mechanics with the idea of trying to provide a quantum description of the brain. In this work we describe some simulations using neuron models by means of which we form simple neural networks that have the capability of oscillation. We analyze the oscillatory activity with root locus method, cross-correlation histograms, and phase planes. In the more complicated neural network models there is the possibility of chaotic oscillatory activity and we study that by means of Lyapunov exponents. The companion paper shows an example of that kind. Author

N95-23142# Lawrence Livermore National Lab., Livermore, CA. **HOW HEALTH RISK FROM RADIATION IS ASSESSED**

L. RAHM-CRITES Jul. 1994 7 p (Contract(s)/Grant(s): W-7405-ENG-48) (DE95-003477; UCRL-ID-118487) Avail: CASI HC A02/MF A01

The likelihood that a dose of radiation will result in death from cancer at some future time can be estimated by multiplying the dose equivalent by a risk factor, or dose-to-risk conversion factor. Conversion factors, which are based on studies of atomic bomb survivors and others, provide approximate predictions of the health effects to be expected from a given radiological exposure. Following recommendations of the Nuclear Regulatory Commission, the Department of Energy currently uses risk conversion factors of 4×10^{-4} (exp -4) (0.0004 LCF's) per person-rem for workers and 5×10^{-4} (exp -4) (0.0005 LCF's) per person-rem for the general public (NRC 1991; DOE 1993). The conversion factor for general public is slightly higher than that for workers because the general public includes infants and children, who are more susceptible to cancer. The current overall death rate from cancer in the United States is between 20 and 25 percent, in other words, cancer accounts for one out of nearly every four deaths. An action affecting a population of 20,000 people, with the estimated potential to induce one latent cancer fatality, should therefore be understood as adding one death from cancer to a normally expected total of 4500. Studies dedicated to improving their ability to predict radiation health effects are constantly in progress, nationally and internationally, and risk conversion factors are periodically revised to incorporate new experimental and epidemiological information. DOE

N95-23780# Stanford Univ., CA. **CELLULAR INTERACTIONS IN THE SUPRACHIASMATIC NUCLEUS Annual Report, 1 May 1993 - 30 Apr. 1994**

ANTHONY N. VANDENPOL May 1994 12 p (Contract(s)/Grant(s): F49620-93-1-0283) (AD-A285639; AFOSR-94-0641TR) Avail: CASI HC A03/MF A01

The technical report examines the progress made in the last year relating to our work on the suprachiasmatic nucleus, the circadian clock in the mammalian hypothalamus. Much of the work examines different aspects of glutamate neurotransmission. Glutamate is probably the transmitter of the retinohypothalamic pathway, and therefore plays an important role in entrainment of circadian rhythms. DTIC

N95-24145# Pacific Northwest Lab., Richland, WA. **BIOLOGICAL INTERACTIONS AND HUMAN HEALTH EFFECTS OF STATIC MAGNETIC FIELDS**

T. S. TENFORDE Sep. 1994 3 p Presented at the Occupational Exposure Limits To Electromagnetic Fields Conference, Stockholm, Sweden, 22-23 Sep. 1994 (Contract(s)/Grant(s): DE-AC06-76RL-01830) (DE95-003147; PNL-SA-24931; CONF-9409253-1) Avail: CASI HC A01/MF A01

Mechanisms through which static magnetic fields interact with living systems will be described and illustrated by selected experimental observations. These mechanisms include electrodynamic interactions with moving ionic charges (blood flow and nerve impulse conduction), magnetomechanical interactions (orientation and translation of molecular structures and magnetic particles), and interactions with electronic spin states in charge transfer reactions (photo-induced electron transfer in photosynthesis). A general summary will also be presented of the biological effects of static magnetic fields studied in the laboratory and in natural settings. One aspect of magnetic field effects that merits special concern is their influence on implanted medical electronic devices such as cardiac pacemakers. Several extensive studies have demonstrated closure of the reed switch in pacemakers exposed to relatively weak static magnetic fields, thereby causing them to revert to an asynchronous mode of operation that is potentially hazardous. Recommendations for human exposure limits are provided. DOE

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BEHAVIORAL SCIENCES

Includes psychological factors; individual and group behavior; crew training and evaluation; and psychiatric research.

N95-22579* National Aeronautics and Space Administration. Langley Research Center, Hampton, VA.

METHOD OF ENCOURAGING ATTENTION BY CORRELATING VIDEO GAME DIFFICULTY WITH ATTENTION LEVEL Patent

ALAN T. POPE, inventor (to NASA) and EDWARD H. BOGART, inventor (to NASA) (Lockheed Engineering and Sciences Co., Hampton, VA.) 27 Dec. 1994 13 p Filed 8 Mar. 1993 Supersedes N93-28128 (31 - 10, p 3085)

(NASA-CASE-LAR-15022-1; US-PATENT-5,377,100; US-PATENT-APPL-SN-029808; US-PATENT-CLASS-364-410; INT-PATENT-CLASS-G06F-15/44) Avail: US Patent and Trademark Office

A method of encouraging attention in persons such as those suffering from Attention Deficit Disorder is provided by correlating the level of difficulty of a video game with the level of attention in a subject. A conventional video game comprises a video display which depicts objects for interaction with a player and a difficulty adjuster which increases the difficulty level, e.g., action speed and/or evasiveness of the depicted object, in a predetermined manner. The electrical activity of the brain is measured at selected sites to determine levels of awareness, e.g., activity in the beta, theta, and alpha states. A value is generated based on this measured electrical signal which is indicative of the level of awareness. The difficulty level of the game is increased as the awareness level value decreases and is decreased as this awareness level value increases.

Official Gazette of the U.S. Patent and Trademark Office

N95-23788# Civil Aeromedical Inst., Oklahoma City, OK.

SOME PERFORMANCE EFFECTS OF AGE AND LOW BLOOD ALCOHOL LEVELS ON A COMPUTERIZED NEUROPSYCHOLOGICAL TEST Final Report

DAVID J. SCHROEDER, HOWARD C. HARRIS, JR., WILLIAM E. COLLINS, and THOMAS E. NESTHUS Feb. 1995 38 p (DOT/FAA/AM-95/7) Avail: CASI HC A03/MF A01

COGSCREEN is a computerized test battery developed for the Federal Aviation Administration as an airman neuropsychological screening instrument for cognitive functioning. This study explored a multifaceted application of the sensitivity of the battery to potential differences in performance capabilities, current civil aviation interest in the performance effects of low levels of blood alcohol, and the potential significance of age on cognitive performance. Nine of 11 basic COGSCREEN tests were used with 60 subjects divided into three age groups, 27-32, 42-47, and 57-62 years. Twelve subjects

within each age category (N=36) comprised an alcohol group, 8 subjects within each age category (N=24) comprised a control group. Subjects were given four 30-minute sessions of training on the task battery during one afternoon and participated in experimental sessions on the next afternoon. Experimental sessions comprised a pre-drinking (baseline) and three post-drinking sessions targeted to breath alcohol (BrAC) levels of 0.04, 0.027, and 0.014 percent for the alcohol group; each control subject received a placebo. The results yielded statistically significant age effects on 20 of 25 measures of performance across the 9 tasks for the pre-drinking sessions favoring the younger age group, using the entire subject population (N=60). An analysis using only the control subject found significant age effects on 18 of the 25 measures of performance on both the baseline and the post-baseline sessions; whereas, the analysis of the alcohol subjects (N=36) found significant age differences on 15 of 25 scores for the pre-drinking session and only 13, 11, and 10 of 25 on the post-drinking sessions respectively. Results of the analyses for age and alcohol session effects revealed statistically significant interactions for 3 measures: mean reaction time of visual comparisons during dual task, and the symbol-digit delayed recall task, as well as the number of correct symbol-digit pairings of the delayed recall task. These data indicate that the COGSCREEN test battery is sensitive to decremental effects on information processing time and cognitive reductions associated with aging. Generally, the results of this study do not support a typical alcohol effect. The simple effects tests yielded results that failed to show sessional patterns consistent with BrAC levels. However, the alcohol sessions may have reduced differences between the age groups. Author

N95-23934# Civil Aeromedical Inst., Oklahoma City, OK.

EFFECTS OF AGE AND LOW DOSES OF ALCOHOL ON COMPENSATORY TRACKING DURING ANGULAR ACCELERATION Final Report

HOWARD C. HARRIS, JR., DAVID J. SCHROEDER, and WILLIAM E. COLLINS Jan. 1995 22 p (DOT/FAA/AM-95/3) Avail: CASI HC A03/MF A01

Heightened interest in existing FAA regulations regarding alcohol and flying, with emphasis on the potential effects of low blood alcohol levels on performance, indicated a need for research to help define effects of low doses of alcohol on performance. This study was designed to assess the effects of age and three breath alcohol levels (0.04, 0.027, and 0.014 percent). Performance was assessed while subjects experienced mild angular stimulation. On the day prior to drinking, 48 subjects drawn from three age categories (27-32, 42-47, and 57-62 years) completed four training sessions on a compensatory tracking task (a localizer/glide slope instrument that required compensatory tracking of both a horizontal and a vertical needle) with and without a secondary auditory recognition task, under 1.0 ft L. and 0.1 ft L. illumination conditions. The test day consisted of a pre-drinking session and three experimental alcohol measurements. Mean performance scores for the three age groups were compared across the four sessions, (pre-drinking and three levels of alcohol). A Multivariate Analysis of Variance (MANOVA) test yielded a significant interaction and a significant mean effect (age and session) for the combined needle errors under the 0.1 ft L. illumination level with the secondary task. The resulting simple effects tests revealed age differences at all post-drinking sessions favoring younger over older subjects, and poorer performance for the older age subjects at the 0.04 percent BrAC level. When testing individual needle errors, MANOVA tests yielded a significant interaction and main effects in the high illumination condition both with and without the secondary task for vertical needle errors. Resulting simple effects Analysis of Variance tests yielded significant age and alcohol effects for the older age subjects. The 0.04 percent level accounted for the alcohol effects. The alcohol and age interaction was accounted for by the older age group at the 0.04 percent BrAC level. This study showed no evidence of performance decrement associated with BrAC's below 0.04 percent. Author

N95-24088# Civil Aeromedical Inst., Oklahoma City, OK.

FUNCTIONS OF EXTERNAL CUES IN PROSPECTIVE MEMORY Final Report

O. U. VORTAC (Oklahoma Univ., Norman, OK.), MARK B. EDWARDS (Oklahoma Univ., Norman, OK.), and CAROL A. MANNING Feb. 1995 16 p

(Contract(s)/Grant(s): DTFA02-91-C-91089)

(DOT/FAA/AM-95/9) Avail: CASI HC A03/MF A01

A simulation of an air traffic control task was the setting for an investigation of the functions of external cues in prospective memory. External cues can support the triggering of an action or memory for the content of the action. We focused on memory of the content and manipulated the temporal characteristics of the external cue to disentangle two possible functions the cue can support: (1) An external cue visible during a retention interval could support rehearsal of the to-be-performed action; and (2) An external cue visible at the end of a retention interval could support retrieval of the to-be-performed action. Two experiments were conducted that converge on the same conclusion: the primary function of an external cue was to support retrieval. Implications for the design of a computer interface to present prospective cues are discussed. Author

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MAN/SYSTEM TECHNOLOGY AND LIFE SUPPORT

Includes human engineering; biotechnology; and space suits and protective clothing.

A95-73427

STANDARDIZATION OF THE GRAPHICAL AND OPERATOR INPUT DEVICE MODULES FOR TACTICAL COMMAND AND CONTROL MAN-MACHINE INTERFACES

CAIREEN E. ALSTON UEC Projects (Pty) Ltd, Cape Town, South Africa, ALBERT H. BROEKSMAN, and MICHAEL R. INGGES IEEE Aerospace and Electronic Systems Magazine (ISSN 0885-8985) vol. 9, no. 11 November 1994 p. 16-20 refs (BTN-95-EIX95122539416) Copyright

Since many of the man-machine interface (MMI) systems designed for tactical command and control operating environments are similar in nature, there is a need to standardize certain elements of the systems. This paper gives a summary of the investigation into standardizing certain graphical MMI elements, and operator input device elements for tactical command and control systems. This standardization allows for rapid prototyping on low-cost platforms, as well as enabling the code to be transferred easily between different operating platforms. Author (EI)

A95-75750

DESIGN AND STRUCTURAL ANALYSIS OF HIGHLY MOBILE SPACE SUITS AND GLOVES

JOHN A. MAIN Vanderbilt Univ, Nashville, TN, United States, STEVEN W. PETERSON, and ALVIN M. STRAUSS Journal of Spacecraft and Rockets (ISSN 0022-4650) vol. 31, no. 6 November-December 1994 p. 1115-1122 refs (BTN-95-EIX95182617479) Copyright

This paper evaluates the factors that control the flexibility of fabric space-suit elements, in particular gloves, by examining a bending model of a pressurized fabric tube. Results from the model are used to evaluate the design strategies used in space-suit components, to evaluate the current direction in research on highly mobile space-suit gloves, and to suggest changes necessary for optimum glove fabric selection. Finally it is shown that the modulus of the fabric used in space-suit joint construction is as important to the flexibility of the joint as the glove size and design. Author (EI)

N95-22513# Dayton Univ. Research Inst., OH.

AVIATOR'S NIGHT VISION IMAGING SYSTEM PREFLIGHT ADJUSTMENT/ASSESSMENT PROCEDURES Final Technical Report, Oct. - Dec. 1993

JOSEPH C. ANTONIO, DEFOREST Q. JORALMON, GEORGE M. FIEDLER, and WILLIAM E. BERKLEY Sep. 1994 23 p

(Contract(s)/Grant(s): F33615-90-C-0005)

(AD-A285829; AL/HR-TR-1994-0111) Avail: CASI HC A03/MF A01

Night vision goggles (NVG's) have been employed in a variety of aircraft for over 20 years. However, only recently has their application begun in fixed-wing fast movers. Research accomplished by the Aircrew Training Research Division of the USAF Armstrong Laboratory demonstrated the loss of NVG performance resulting from improper adjustments. This report describes correct adjustment procedures for the Aviator's Night Vision Imaging System, or ANVIS. The procedures described were developed so aircrews could take advantage of the adjustments available on the NVG's. Additionally, image descriptions are given to help aircrews evaluate NVG performance. Information on the proper equipment/pace needed for proper evaluation is also included. DTIC

N95-22766* National Aeronautics and Space Administration. Lyndon B. Johnson Space Center, Houston, TX.

METHOD FOR FORMING A GLOVE ATTACHMENT Patent

FREDERIC S. DAWN, inventor (to NASA), WALTER W. GUY, inventor (to NASA), JOSEPH KOSMO, inventor (to NASA), ARTHUR P. DRENNAN, inventor (to NASA), and RICHARD P. TSCHIRCH, inventor (to NASA) 24 Jan. 1995 6 p Filed 14 Aug. 1992 Supersedes N92-34210 (30 - 24, p 4222)

(NASA-CASE-MSC-21632-1; US-PATENT-5,384,083; US-PATENT-APPL-SN-929556; US-PATENT-CLASS-264-130; US-PATENT-CLASS-264-135; US-PATENT-CLASS-264-137; US-PATENT-CLASS-264-257; INT-PATENT-CLASS-B29C-39/12; INT-PATENT-CLASS-B29C-67/14) Avail: US Patent and Trademark Office

An attachment principally for the palm of an astronaut glove to enhance the gripping area of the palm without detracting from the flexibility and utility of the glove is presented. The attachment is a composite construction formed from a layer of silicone rubber having an outer surface with a friction configuration and another layer of silicone rubber in which a Nomex Aramid mesh fabric is embedded prior to curing. The method of construction involves the use of a mold with a friction configuration surface. A first layer of silicone rubber or sealant is disposed in the mold and allowed to set for an hour. A second layer of silicone rubber or sealant is layered over the first layer and leveled. A Nomex Aramid mesh fabric is embedded into the second layer and the composite is permitted to cure. When cured, a configured area of the composite construction is glued or stitched to the palm area of the glove.

Official Gazette of the U.S. Patent and Trademark Office

N95-22797* Georgia Inst. of Tech., Atlanta, GA. Center for Human-Machine Systems Research.

HUMAN-CENTERED DESIGN OF HUMAN-COMPUTER-HUMAN DIALOGS IN AEROSPACE SYSTEMS Semiannual Report No. 2, 1 Feb. - 31 Jul. 1994

CHRISTINE M. MITCHELL 31 Jul. 1994 13 p

(Contract(s)/Grant(s): NCC2-824)

(NASA-CR-197379; NAS 1.26:197379; E-24-X30) Avail: CASI HC A03/MF A01

The second six months of this grant saw further development of GT-CATS, the Georgia Tech Crew Activity Tracking System, and progress on research exploring tutoring concepts for tutors for mode management. The latter included data analysis and a preliminary paper summarizing the development and evaluation of the VNAV Tutor. A follow-on to the VNAV Tutor is planned. Research in this direction will examine the use of OFMspert and GT-CATS to create an 'intelligent' tutor for mode management, a more extensive domain of application than only vertical navigation, and alternative

pedagogy, such as substituting focused 'cases' of reported mode management situations rather than lessons defined by full LOFT scenarios.
Derived from text

N95-23194* Jet Propulsion Lab., California Inst. of Tech., Pasadena, CA.

LIFE SUPPORT SYSTEMS ANALYSIS AND TECHNICAL TRADES FOR A LUNAR OUTPOST Report, Oct. 1993

J. F. FERRALL, G. B. GANAPATHI, N. K. ROHATGI, and P. K. SESHAN Dec. 1994 109 p
(NASA-TM-109927; NAS 1.15:109927) Avail: CASI HC A06/MF A02

The NASA/JPL life support systems analysis (LISSA) software tool was used to perform life support system analysis and technology trades for a Lunar Outpost. The life support system was modeled using a chemical process simulation program on a steady-state, one-person, daily basis. Inputs to the LISSA model include metabolic balance load data, hygiene load data, technology selection, process operational assumptions and mission parameter assumptions. A baseline set of technologies has been used against which comparisons have been made by running twenty-two cases with technology substitutions. System, subsystem, and technology weights and powers are compared for a crew of 4 and missions of 90 and 600 days. By assigning a weight value to power, equivalent system weights are compared. Several less-developed technologies show potential advantages over the baseline. Solid waste treatment technologies show weight and power disadvantages but one could have benefits associated with the reduction of hazardous wastes and very long missions. Technology development towards reducing the weight of resupplies and lighter materials of construction was recommended. It was also recommended that as technologies are funded for development, contractors should be required to generate and report data useful for quantitative technology comparisons. Author

N95-23264* National Aeronautics and Space Administration. Ames Research Center, Moffett Field, CA.

SELF-GENERATING OSCILLATING PRESSURE EXERCISE DEVICE Patent

DONALD E. WATENPAUGH, inventor (to NASA) 18 Oct. 1994 8 p Filed 13 May 1993

(NASA-CASE-ARC-12000-1; US-PATENT-5,356,361; US-PATENT-APPL-SN-061401; US-PATENT-CLASS-482-111; US-PATENT-CLASS-601-23; INT-PATENT-CLASS-A63B-21/008) Avail: US Patent and Trademark Office

An exercise device, especially suitable for zero gravity workouts, has a collapsible chamber which generates negative pressure on the lower portion of a body situated therein. The negative pressure is generated by virtue of leg, hand and shoulder interaction which contracts and expands the chamber about the person and by virtue of air flow regulation by valve action.

Official Gazette of the U.S. Patent and Trademark Office

N95-23274* National Aeronautics and Space Administration. Lyndon B. Johnson Space Center, Houston, TX.

LIVING IN SPACE (Videotape)

RAY BROWN, ed. 1993 Its Liftoff to Learning Series Videotape: 9 min. 45 sec. playing time, in color, with sound
(NASA-TM-110536; NONP-NASA-VT-95-43939) Avail: CASI VHS A02/BETA A22

In this educational video from the 'Liftoff to Learning' series, astronauts from the STS-56 Mission (Ken Cockrell, Mike Foale, Ellen Ochoa, Steve Oswald, and Ken Cameron) explain and show through demonstrations how microgravity affects the way astronauts live onboard the Space Shuttle, and how these same daily habits or processes differ on Earth. A tour of the Space Shuttle is given, including the sleeping compartments, the kitchen area, the storage compartments, and the Waste Collection System (or WCS, as they call it). Daily habits (brushing teeth, shampooing hair and bathing, eating,...) are explained and actively illustrated, along with reasons of how these applications differ from their employment on Earth. CASI

N95-23474* Lamar Univ., Beaumont, TX. Dept. of Chemical Engineering.

RESOURCE RECOVERY AND EPIDEMIOLOGY OF ANAEROBIC WASTEWATER TREATMENT PROCESS IN A CONTROLLED ECOLOGICAL LIFE SUPPORT SYSTEM Final Report

KU-YEN LI and MADELYN D. HUNT 27 Feb. 1995 121 p
(Contract(s)/Grant(s): NAG9-696)
(NASA-CR-197930; NAS 1.26:197930) Avail: CASI HC A06/MF A02

The results of work accomplished under two different areas: (1) Resource Recovery of an Anaerobic Wastewater Treatment process, and (2) Epidemiological Study of an Anaerobic Wastewater Treatment Process are documented. The first part of the work was to set up and test three anaerobic digesters and then run these three digesters with a NASA-simulated wastewater. The second part of the work was to use a multi-drug resistant strain of *Salmonella choleraesuis* as the indicator bacteria for the epidemiological study. Details of these two parts can be found in two master's theses and are described in Sections 3 and 4 of this report. Several important results condensed from these two parts are summarized in Section 2. Author

N95-23601* Advisory Group for Aerospace Research and Development, Neuilly-Sur-Seine (France). Guidance and Control Panel.

KNOWLEDGE-BASED GUIDANCE AND CONTROL FUNCTIONS [APPLICATION DES SYSTEMES EXPERTS POUR LE GUIDAGE ET LE PILOTAGE]

Jan. 1995 183 p
(AGARD-AR-325; ISBN-92-836-1009-1) Copyright Avail: CASI HC A09/MF A02

This report summarizes the deliberations of Working Group 11 of the Guidance and Control Panel of AGARD. The objectives of the Working Group are: (1) analyze the structure of knowledge-based guidance and control functions related to aircraft, missions, and the battlefield and identify their potential for automation; (2) analyze the structure of knowledge-based guidance and control functions related to the life cycle of guidance and control systems, and identify their potential for automation; (3) review the state-of-the-art of those software and hardware oriented technologies required for the transfer of the knowledge-based G&C functions to automatic systems; (4) review existing programs; and (5) make recommendations for future work. Author

N95-23704* Ministry of International Trade and Industry, Tsukuba (Japan). Electromechanical Lab.

DEVELOPMENT OF ADVANCED ROBOTIC HAND SYSTEM FOR SPACE APPLICATION

KAZUO MACHIDA, KENZO AKITA (Institute for Unmanned Space Experiments Free Flyer, Tokyo, Japan.), TATSUO MIKAMI (Fujitsu Ltd., Kawasaki, Japan.), and SATORU KOMADA (Fujitsu Ltd., Kawasaki, Japan.) In JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 165-168 Oct. 1994

Avail: CASI HC A01/MF A03

The Advanced Robotic Hand System (ARH) is a precise telerobotics system with a semi dexterous hand for future space application. The ARH will be tested in space as one of the missions of the Engineering Tests Satellite 7 (ETS-7) which will be launched in 1997. The objectives of the ARH development are to evaluate the capability of a possible robot hand for precise and delicate tasks and to validate the related technologies implemented in the system. The ARH is designed to be controlled both from ground as a teleoperation and by locally autonomous control. This paper presents the overall system design and the functional capabilities of the ARH as well as its mission outline as the preliminary design has been completed. Author

N95-23705* Fujitsu Ltd., Kawasaki (Japan).

A THREE-FINGER MULTISENSORY HAND FOR DEXTEROUS SPACE ROBOTIC TASKS

YUICHI MURASE, SATORU KOMADA, TAKASHI UCHIYAMA,

KAZUO MACHIDA (Ministry of International Trade and Industry, Tsukuba, Japan.), and KENZO AKITA (Institute for Unmanned Space Experiments Free Flyer, Tokyo, Japan.) *In* JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 169-172 Oct. 1994
 Avail: CASI HC A01/MF A03

The National Space Development Agency of Japan will launch ETS-7 in 1997, as a test bed for next generation space technology of RV&D and space robot. MITI has been developing a three-finger multisensory hand for complex space robotic tasks. The hand can be operated under remote control or autonomously. This paper describes the design and development of the hand and the performance of a breadboard model. Author

N95-23707*# Centre National d'Etudes Spatiales, Toulouse (France).

ROBOTIC EXPERIMENT WITH A FORCE REFLECTING HANDCONTROLLER ONBOARD MIR SPACE STATION

M. DELPECH and Y. MATZAKIS (MATRA Marconi Space, Toulouse, France.) *In* JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 177-181 Oct. 1994

Avail: CASI HC A01/MF A03

During the French CASSIOPEE mission that will fly onboard MIR space station in 1996, ergonomic evaluations of a force reflecting handcontroller will be performed on a simulated robotic task. This handcontroller is a part of the COGNILAB payload that will be used also for experiments in neurophysiology. The purpose of the robotic experiment is the validation of a new control and design concept that would enhance the task performances for telemanipulating space robots. Besides the handcontroller and its control unit, the experimental system includes a simulator of the slave robot dynamics for both free and constrained motions, a flat display screen and a seat with special fixtures for holding the astronaut. Author

N95-23708*# National Space Development Agency, Tsukuba (Japan). Space Station Dept.

DEVELOPMENT OF JAPANESE EXPERIMENT MODULE REMOTE MANIPULATOR SYSTEM

TATSUO MATSUEDA, FUMIHIRO KUWAO (Toshiba Corp., Kawasaki, Japan.), SHOICHI MOTOHASI (Toshiba Corp., Kawasaki, Japan.), and RYO OKAMURA (Toshiba Corp., Kawasaki, Japan.) *In* JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 183-186 Oct. 1994

Avail: CASI HC A01/MF A03

National Space Development Agency of Japan (NASDA) is developing the Japanese Experiment Module (JEM), as its contribution to the International Space Station. The JEM consists of the pressurized module (PM), the exposed facility (EF), the experiment logistics module pressurized section (ELM-PS), the experiment logistics module exposed section (ELM-ES) and the Remote Manipulator System (RMS). The JEMRMS services for the JEM EF, which is a space experiment platform, consists of the Main Arm (MA), the Small Fine Arm (SFA) and the RMS console. The MA handles the JEM EF payloads, the SFA and the JEM element, such as ELM-ES. Derived from text

N95-23709*# Toshiba Corp., Kawasaki (Japan). Space Systems Engineering Dept.

ROBOT ARM SYSTEM FOR AUTOMATIC SATELLITE CAPTURE AND BERTHING

SHINICHIRO NISHIDA, HIDETOSHI TORIU, MASATO HAYASHI, TOMOAKI KUBO, and MAKOTO MIYATA *In* JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 187-190 Oct. 1994

Avail: CASI HC A01/MF A03

Load control is one of the most important technologies for capturing and berthing free flying satellites by a space robot arm because free flying satellites have different motion rates. The performance of active compliance control techniques depend on the

location of the force sensor and the arm's structural compliance. A compliance control technique for the robot arm's structural elasticity and a consideration for an end-effector appropriate for it are presented in this paper. Author

N95-23714*# Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek, The Hague (Netherlands). Physics and electronics Lab.
POINTER: PORTABLE INTELLIGENT TRAINER FOR EXTERNAL ROBOTICS

HILBERT KUIPER and PATRICK J. RIKKEN *In* JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 209-212 Oct. 1994

Avail: CASI HC A01/MF A03

Intelligent tutoring systems (ITS's) play an increasing role in training and education of people with different levels of skill and knowledge. As compared to conventional computer based training (CBT) an ITS provides more tailored instruction by trying to mimic the teaching behavior of a human instructor as much as possible and is therefore much more flexible. This paper starts with an introduction to ITS's, followed by the description of an ITS for training of an (astronaut) operator in monitoring and controlling robotic arm procedures. The robotic arm will be used for exchange of equipment between a space station and a space plane involving critical and accurate movements of the robotic arm. The ITS for this application, called Pointer, is developed by TNO Physics and Electronics Laboratory and is based upon an existing ITS that includes procedural training. Pointer has been developed on a workstation whereas the target platform was a portable computer. Therefore, a lot of attention had to be paid to scaling effects and keeping up with user friendliness of the much smaller user interface. Although the learning domain was the control of a robotic arm, it is clear that use of intelligent training technologies on a portable computer has many other applications (payload operations, operation control rooms, etc.). Training can occur at any time and place in an attractive and cost effective way. Author

N95-23715*# National Space Development Agency, Tsukuba (Japan). Space Experiment Dept.

AUTOMATION AND CREW TIME SAVING IN THE SPACE EXPERIMENT

KOHTARO MATSUMOTO, TSUYOSHI SUZUKI, KOUICHI FUNAYA (NEC Corp., Kawasaki, Japan.), TAKEYA KAWAMURA (Mitsubishi Heavy Industries Ltd., Wadasaki, Japan.), and MASAYOSHI SONOBE (Hitachi Ltd., Japan.) *In* JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 215-218 Oct. 1994

Avail: CASI HC A01/MF A03

We describe preliminary results of the feasibility study of automation and crew workload saving in space experiments on the space station. Some functions have been studied that can be automated within a single rack and without major impact to the development process and costs. In addition, we assume the following premises: (1) applicable as the second generation apparatuses; (2) maximum reduction of the crew workload; and (3) automation between racks including storage. Four apparatuses have been selected as the study case; results for three are summarized. Derived from text

N95-23720*# MATRA Marconi Space, Toulouse (France).

FORMALIZING PROCEDURES FOR OPERATIONS AUTOMATION, OPERATOR TRAINING AND SPACECRAFT AUTONOMY

FRANCOIS LECOUCAT and ARNAUD DESAINTVINCENT *In* JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994 p 239-242 Oct. 1994

Avail: CASI HC A01/MF A03

The generation and validation of operations procedures is a key task of mission preparation that is quite complex and costly. This has motivated the development of software applications providing support for procedures preparation. Several applications have been developed at MATRA MARCONI SPACE (MMS) over the last five

years. They are presented in the first section of this paper. The main idea is that if procedures are represented in a formal language, they can be managed more easily with a computer tool and some automatic verifications can be performed. One difficulty is to define a formal language that is easy to use for operators and operations engineers. From the experience of the various procedures management tools developed in the last five years (including the POM, EOA, and CSS projects), MMS has derived OPSMAKER, a generic tool for procedure elaboration and validation. It has been applied to quite different types of missions, ranging from crew procedures (PREVISE system), ground control centers management procedures (PROCSU system), and - most relevant to the present paper - satellite operation procedures (PROCSAT developed for CNES, to support the preparation and verification of SPOT 4 operation procedures, and OPSAT for MMS telecom satellites operation procedures).

Derived from text

N95-23723*# National Aeronautics and Space Administration. Lyndon B. Johnson Space Center, Houston, TX.
DEXTEROUS ORBITAL SERVICING SYSTEM (DOSS)
 CHARLES R. PRICE, REGINALD B. BERKA, and JOHN T. CHLADEK
In JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994
 p 257-260 Oct. 1994
 Avail: CASI HC A01/MF A03

The Dexterous Orbiter Servicing System (DOSS) is a dexterous robotic spacecraft system that is based on the manipulator designed as part of the Flight Telerobotics Servicer program for the Space Station Freedom and built during a 'technology capture' effort that was commissioned when the FTS was cancelled from the Space Station Freedom program. The FTS technology capture effort yielded one flight manipulator and the 1 g hydraulic simulator that had been designed as an integrated test tool and crew trainer. The DOSS concept was developed to satisfy needs of the telerobotics research community, the space shuttle, and the space station. As a flight testbed, DOSS would serve as a baseline reference for testing the performance of advanced telerobotics and intelligent robotics components. For shuttle, the DOSS, configured as a movable dexterous tool, would be used to provide operational flexibility for payload operations and contingency operations. As a risk mitigation flight demonstration, the DOSS would serve the International Space Station to characterize the end to end system performance of the Special Purpose Dexterous Manipulator performing assembly and maintenance tasks with actual ISSA orbital replacement units. Currently, the most likely entrance of the DOSS into spaceflight is a risk mitigation flight experiment for the International Space Station.

Author

N95-23732*# Italian Space Agency, Rome.
PLANETARY STATIONS AND ABYSSAL BENTHIC LABORATORIES: AN OVERVIEW OF PARALLEL APPROACHES FOR LONG-TERM INVESTIGATION IN EXTREME ENVIRONMENTS
 S. DIPIPPO, W. PRENDIN (Tecnomare S.p.A., Italy.), and F. GASPARONI (Tecnomare S.p.A., Italy.) *In JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994* p 301-304 Oct. 1994
 Avail: CASI HC A01/MF A03

In spite of the apparent great differences between deep ocean and space environment, significant similarities can be recognized when considering the possible solutions and technologies enabling the development of remote automatic stations supporting the execution of scientific activities. In this sense it is believed that mutual benefits shall be derived from the exchange of experiences and results between people and organizations involved in research and engineering activities for hostile environments, such as space, deep sea, and polar areas. A significant example of possible technology transfer and common systematic approach is given, which describes in some detail how the solutions and the enabling technologies identified for an Abyssal Benthic Laboratory can be applied for the case of a lunar or planetary station.

Author

N95-23735*# National Aeronautics and Space Administration. Lyndon B. Johnson Space Center, Houston, TX.

TELEPRESENCE CONTROL OF A DUAL-ARM DEXTEROUS ROBOT

LARRY LI, BRIAN COX (Lockheed Engineering and Sciences Co., Houston, TX.), SUSAN SHELTON (Lockheed Engineering and Sciences Co., Houston, TX.), and MYRON DIFTLER (Lockheed Engineering and Sciences Co., Houston, TX.) *In JPL, Third International Symposium on Artificial Intelligence, Robotics, and Automation for Space 1994* p 313-316 Oct. 1994
 Avail: CASI HC A01/MF A03

Telepresence is an approach to teleoperation that provides egocentric, intuitive interactions between an operator and a remote environment. This approach takes advantage of the natural cognitive and sensory-motor skills of an on-orbit crew and effectively transfers them to a slave robot. A dual-arm dexterous robot operating under telepresence control has been developed and is being evaluated. Preliminary evaluation revealed several important observations that suggest the directions of future enhancement. Author

N95-24021# Wichita State Univ., Wichita, KS. National Inst. for Aviation Research.

DESIGN OF A CERVICAL SPINE GROSS MOTION SIMULATOR FOR STANDARD SIZE HUMAN AND ANTHROPOMORPHIC DUMMY ADULT AND CHILD
 SRINIVAS REDDY MALAPATI Sep. 1994 161 p
 (NIAR-94-16) Avail: CASI HC A08/MF A02

In the field of automotive and aircraft safety research, simulation of crashes to study the effect on the human body is vital in order to evaluate and improve crash safety devices and occupant environment. Realistic simulation of the neck response in a dummy is of vital importance to get a human-like dynamical behavior of the head. Trajectories of the head and the nature of the head contact with vehicle interior or exterior are critically dependent on the dummy's neck design. Most of this work is done by way of experiments, using instrumented dummies, cadavers, and occasionally animals or volunteers. In the sixties, fast digital computers together with advanced mathematical techniques led to a new method of simulations with mathematical models. These models have the advantage that a great number of simulation results can be obtained easily, without any measurement problems as occur with experiments. This thesis describes the development and validation of two-dimensional, nine degree-of-freedom mathematical models which simulate the dynamic responses of the head-neck assembly of a 50th percentile male human and a three-year-old child. The validation of the three-year-old child head-neck model is made by comparing the results with the simple single hinge-type head-neck model of a three-year-old child dummy in the code MADYMO frequently used by the automobile industries for prediction of potential injuries to vehicle occupants as a result of crash. Sensitivity studies are conducted and model performances are evaluated. Comparison between child and adult responses were made and significant differences were noticed. Numerous similarities between the model response and experimental performance suggest that the models have considerable potential as a design tool.

Author

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SPACE BIOLOGY

Includes exobiology; planetary biology; and extraterrestrial life.

A95-75050
COSMIC EVOLUTION OF THE BIOGENIC ELEMENTS AND COMPOUNDS

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This paper traces the evolution of the biogenic elements H, C, N, O, P and S from their creation by cosmic nucleosynthesis to their inclusion in living systems on the surface of the Earth. Evidence for the presence of significant prebiotic molecules in interstellar clouds and in primitive meteorites is reviewed. The possible relevance of this discovery to the origin of life on Earth is assessed in the light of evidence suggesting that such molecules could not be synthesized in a primitive CO₂-dominated terrestrial atmosphere.

Author (Hemer)

A95-76885

OBSERVATION OF A MASS INDEPENDENT OXYGEN ISOTOPIC COMPOSITION IN TERRESTRIAL STRATOSPHERIC CO₂, THE LINK TO OZONE CHEMISTRY, AND THE POSSIBLE OCCURRENCE IN THE MARTIAN ATMOSPHERE

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Multi-isotope ($\delta^{17}\text{O}$ and $\delta^{18}\text{O}$) measurements of stratospheric CO₂ and (14)CO are reported. Samples were acquired from altitudes in excess of 11.5 km from Christchurch, New Zealand to the South Pole. A mass independent isotopic variation is observed in CO₂, the magnitude of which correlates well with (14)CO concentration, indicating a stratospheric source of the effect. The component arises from isotopic exchange between the product of O₃ photolysis, O(1D) and CO₂, thus providing a unique measure of ozone photolysis and turnover. A similar process may occur in the Martian atmosphere, as suggested by water isotopic measurements from SNC meteorites.

Author (Hemer)

A95-77124

FAR-INFRARED SPECTROSCOPY OF CO₂ CLATHRATE HYDRATE WITH MARTIAN APPLICATIONS

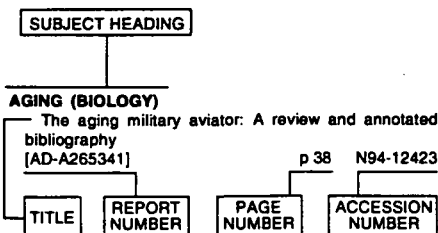
JOSEPH C. LANDRY Univ. of Michigan, MI, US and ANTHONY W. ENGLAND Univ. of Michigan, MI, US Geophysical Research Letters (ISSN 0094-8276) vol. 21, no. 25 December 15, 1994 p. 2829-2832

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It has been suggested that CO₂ clathrate hydrate forms in the Martian polar regions in winter. A large deposit of hydrate would affect the polar energy budget because of its low thermal conductivity and its sizeable latent heat of dissociation, and it could also be important to the total CO₂ budget. In this paper we present the far-infrared spectrum of CO₂ hydrate at 150 K. The spectrum exhibits a broad absorption centered near 17/cm (0.59 mm) that is probably due to a rattling transition. Our radiative transfer model predicts that the absorption gives rise to a distinctive emission spectrum for densely packed particles having average diameters greater than 100 microns.

Author (Hemer)

Typical Subject Index Listing



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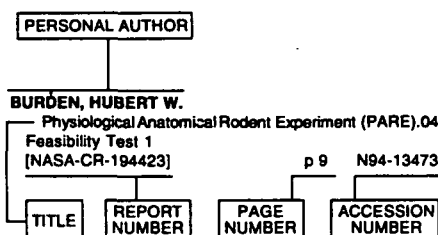
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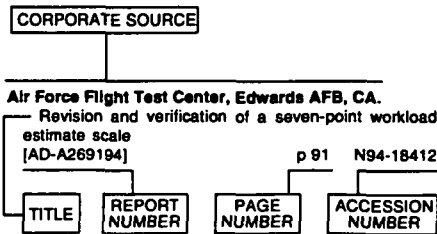
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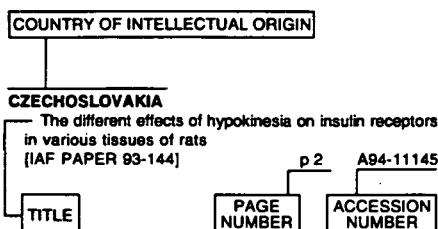
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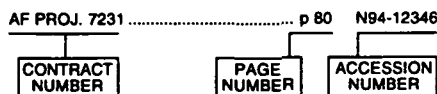
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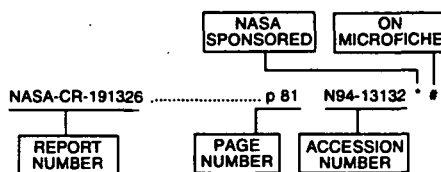
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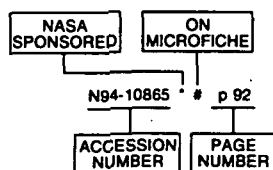
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(913) 864-4660 Fax: (913) 864-3855

KENTUCKY

UNIV. OF KENTUCKY

King Library South
Govt. Publications/Maps Dept.
Patterson Drive
Lexington, KY 40506-0039
(606) 257-3139 Fax: (606) 257-3139

LOUISIANA

LOUISIANA STATE UNIV.

Middleton Library
Govt. Documents Dept.
Baton Rouge, LA 70803-3312
(504) 388-2570 Fax: (504) 388-6992

LOUISIANA TECHNICAL UNIV.

Prescott Memorial Library
Govt. Documents Dept.
Ruston, LA 71272-0046
(318) 257-4962 Fax: (318) 257-2447

MAINE

UNIV. OF MAINE

Raymond H. Fogler Library
Govt. Documents Dept.
Orono, ME 04469-5729
(207) 581-1673 Fax: (207) 581-1653

MARYLAND

UNIV. OF MARYLAND - COLLEGE PARK

McKeldin Library
Govt. Documents/Maps Unit
College Park, MD 20742
(301) 405-9165 Fax: (301) 314-9416

MASSACHUSETTS

BOSTON PUBLIC LIBRARY

Govt. Documents
666 Boylston Street
Boston, MA 02117-0286
(617) 536-5400, ext. 226
Fax: (617) 536-7758

MICHIGAN

DETROIT PUBLIC LIBRARY

5201 Woodward Avenue
Detroit, MI 48202-4093
(313) 833-1025 Fax: (313) 833-0156

LIBRARY OF MICHIGAN

Govt. Documents Unit
P.O. Box 30007
717 West Allegan Street
Lansing, MI 48909
(517) 373-1300 Fax: (517) 373-3381

MINNESOTA

UNIV. OF MINNESOTA

Govt. Publications
409 Wilson Library
309 19th Avenue South
Minneapolis, MN 55455
(612) 624-5073 Fax: (612) 626-9353

MISSISSIPPI

UNIV. OF MISSISSIPPI

J.D. Williams Library
106 Old Gym Bldg.
University, MS 38677
(601) 232-5857 Fax: (601) 232-7465

MISSOURI

UNIV. OF MISSOURI - COLUMBIA

106B Ellis Library
Govt. Documents Sect.
Columbia, MO 65201-5149
(314) 882-6733 Fax: (314) 882-8044

MONTANA

UNIV. OF MONTANA

Mansfield Library
Documents Division
Missoula, MT 59812-1195
(406) 243-6700 Fax: (406) 243-2060

NEBRASKA

UNIV. OF NEBRASKA - LINCOLN

D.L. Love Memorial Library
Lincoln, NE 68588-0410
(402) 472-2562 Fax: (402) 472-5131

NEVADA

THE UNIV. OF NEVADA LIBRARIES

Business and Govt. Information
Center
Reno, NV 89557-0044
(702) 784-6579 Fax: (702) 784-1751

NEW JERSEY

NEWARK PUBLIC LIBRARY

Science Div. - Public Access
P.O. Box 630
Five Washington Street
Newark, NJ 07101-7812
(201) 733-7782 Fax: (201) 733-5648

NEW MEXICO

UNIV. OF NEW MEXICO

General Library
Govt. Information Dept.
Albuquerque, NM 87131-1466
(505) 277-5441 Fax: (505) 277-6019

NEW MEXICO STATE LIBRARY

325 Don Gaspar Avenue
Santa Fe, NM 87503
(505) 827-3824 Fax: (505) 827-3888

NEW YORK

NEW YORK STATE LIBRARY

Cultural Education Center
Documents/Gift & Exchange Section
Empire State Plaza
Albany, NY 12230-0001
(518) 474-5355 Fax: (518) 474-5786

NORTH CAROLINA

UNIV. OF NORTH CAROLINA - CHAPEL HILL

Walter Royal Davis Library
CB 3912, Reference Dept.
Chapel Hill, NC 27514-8890
(919) 962-1151 Fax: (919) 962-4451

NORTH DAKOTA

NORTH DAKOTA STATE UNIV. LIB.

Documents
P.O. Box 5599
Fargo, ND 58105-5599
(701) 237-8886 Fax: (701) 237-7138

UNIV. OF NORTH DAKOTA

Chester Fritz Library
University Station
P.O. Box 9000 - Centennial and
University Avenue
Grand Forks, ND 58202-9000
(701) 777-4632 Fax: (701) 777-3319

OHIO

STATE LIBRARY OF OHIO

Documents Dept.
65 South Front Street
Columbus, OH 43215-4163
(614) 644-7051 Fax: (614) 752-9178

OKLAHOMA

OKLAHOMA DEPT. OF LIBRARIES

U.S. Govt. Information Division
200 Northeast 18th Street
Oklahoma City, OK 73105-3298
(405) 521-2502, ext. 253
Fax: (405) 525-7804

OKLAHOMA STATE UNIV.

Edmon Low Library
Stillwater, OK 74078-0375
(405) 744-6546 Fax: (405) 744-5183

OREGON

PORTLAND STATE UNIV.

Branford P. Millar Library
934 Southwest Harrison
Portland, OR 97207-1151
(503) 725-4123 Fax: (503) 725-4524

PENNSYLVANIA

STATE LIBRARY OF PENN.

Govt. Publications Section
116 Walnut & Commonwealth Ave.
Harrisburg, PA 17105-1601
(717) 787-3752 Fax: (717) 783-2070

SOUTH CAROLINA

CLEMSON UNIV.

Robert Muldrow Cooper Library
Public Documents Unit
P.O. Box 343001
Clemson, SC 29634-3001
(803) 656-5174 Fax: (803) 656-3025

UNIV. OF SOUTH CAROLINA

Thomas Cooper Library
Green and Sumter Streets
Columbia, SC 29208
(803) 777-4841 Fax: (803) 777-9503

TENNESSEE

UNIV. OF MEMPHIS LIBRARIES

Govt. Publications Dept.
Memphis, TN 38152-0001
(901) 678-2206 Fax: (901) 678-2511

TEXAS

TEXAS STATE LIBRARY

United States Documents
P.O. Box 12927 - 1201 Brazos
Austin, TX 78701-0001
(512) 463-5455 Fax: (512) 463-5436

TEXAS TECH. UNIV. LIBRARIES

Documents Dept.
Lubbock, TX 79409-0002
(806) 742-2282 Fax: (806) 742-1920

UTAH

UTAH STATE UNIV.

Merrill Library Documents Dept.
Logan, UT 84322-3000
(801) 797-2678 Fax: (801) 797-2677

VIRGINIA

UNIV. OF VIRGINIA

Alderman Library
Govt. Documents
University Ave. & McCormick Rd.
Charlottesville, VA 22903-2498
(804) 824-3133 Fax: (804) 924-4337

WASHINGTON

WASHINGTON STATE LIBRARY

Govt. Publications
P.O. Box 42478
16th and Water Streets
Olympia, WA 98504-2478
(206) 753-4027 Fax: (206) 586-7575

WEST VIRGINIA

WEST VIRGINIA UNIV. LIBRARY

Govt. Documents Section
P.O. Box 6069 - 1549 University Ave.
Morgantown, WV 26506-6069
(304) 293-3051 Fax: (304) 293-6638

WISCONSIN

ST. HIST. SOC. OF WISCONSIN LIBRARY

Govt. Publication Section
816 State Street
Madison, WI 53706
(608) 264-6525 Fax: (608) 264-6520

MILWAUKEE PUBLIC LIBRARY

Documents Division
814 West Wisconsin Avenue
Milwaukee, WI 53233
(414) 286-3073 Fax: (414) 286-8074

National Aeronautics and
Space Administration
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Washington, DC 20546-0001